priority 9/25/92

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     (FILE 'HOME' ENTERED AT 08:32:18 ON 20 JAN 2004)
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     FILE 'REGISTRY' ENTERED AT 08:33:43 ON 20 JAN 2004
L1             1 S TAXOL/CN
L2            62 S 33069-62-4/CRN

     FILE 'HCAPLUS' ENTERED AT 08:36:48 ON 20 JAN 2004
L3          7962 S L1 OR L2
L4         10727 S TAXOL OR PACLITAXEL OR PLAXICEL OR YEWTAXAN# OR TAXALBIN# OR
                  E STENT/CT
                  E E10+ALL
L5          1534 S E2
L6          2466 S STENT
                  E BLOOD VESSEL/CT
L7          9801 S E41
L8         22486 S VASCULAR(L)SMOOTH(L)MUSCLE
L9         15220 S VASCULAR(L)SMOOTH(L)MUSCLE(L)CELL
                  E ANGIOPLASTY/CT
                  E E3+ALL
L10         2708 S E2
                  E ANGIOPLAST
L11         4247 S E9
                  E RESTENOSIS/CT
                  E E3+ALL
L12         3406 S E2,E3
L13         5196 S RESTENOSIS
                  E STENOSIS/CT
L14            6 S E3
                  E E2+ALL
L15         1013 S E12
                  E MUSCLE CELL/CT
                  E CELL MIGRATION/CT
L16        15070 S E3
                  E E3+ALL
                  E E10+ALL
                  E PROSTHE/CT
L17        27060 S E36,E37
L18         1078 S E66,E67
L19          316 S E62
L20           32 S E43
L21        12082 S E57
                  E E37+ALL
                  E IMPLANT/CT
                  E E12+ALL
L22         1837 S E2
L23        12082 S E8
                  E CATHETER/CT
L24          104 S E5
                  E E5+ALL
L25         2425 S E2
L26          147 S L3 AND L5,L6,L17-L25
L27          143 S L3 AND L7-L15
L28           34 S L3 AND L16
L29          165 S L4 AND L5,L6,L17-L25
L30          171 S L4 AND L7-L15
L31          522 S L7 AND L16
L32           76 S L26,L29 AND L27,L28,L30,L31
L33           72 S L3,L4 AND SUSTAIN?(L)RELEAS?
L34          282 S L3,L4 AND (SUSTAIN? OR CONTROL?)(L)(RELEAS? OR ACTION?)
L35           24 S L33,L34 AND L32
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                E SCIMED/PA,CS
L36          216 S E3-E22
                E KUNZ L/AU
L37           72 S E3,E6,E11,E12
                E KLEIN R/AU
L38          418 S E3,E4
L39           41 S E60,E62,E63
                E RENO J/AU
L40           95 S E3,E5,E8,E12,E13
                E GRAINGER D/AU
L41           82 S E3,E5,E8,E11,E12
                E METCALFE J/AU
L42          302 S E3,E6,E14,E15
                E WEISSBERG P/AU
L43           80 S E3-E6
                E ANDERSON P/AU
L44          131 S E3,E14
                E ANDERSON PETE/AU
L45           61 S E3,E4,E10
L46           18 S L36-L45 AND L3,L4
L47           14 S L46 AND L5-L35
L48            4 S L46 NOT L47
L49            1 S L48 AND STRUT
L50           15 S L47,L49
L51           34 S L35,L50
L52           27 S L51 AND ?POLYM?
L53            9 S L51 AND ?BIODEGRAD?
L54            5 S L51 AND ?BIOCOMPAT?
L55           10 S L52 AND L53,L54
L56            4 S L51-L55 AND (PY<=1992 OR PRY<=1992 OR AY<=1992)
L57           26 S L26-L35 AND (PY<=1992 OR PRY<=1992 OR AY<=1992)
L58           22 S L57 NOT L51
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L59            4 S E1-E12
L60            8 S L56,L59 AND L3-L59
L61           30 S L51 AND L3-L50,L52-L59 NOT L60

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FILE LAST UPDATED: 19 Jan 2004  (20040119/ED)

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L60 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:348781 HCAPLUS
DN 138:343976
ED Entered STN: 08 May 2003
TI Method of preparing a tissue sealant-treated biomedical material
IN Burgess, Willson H.; Greisler, Howard P.; Drohan, William N.; Maciag, Thomas; MacPhee, Martin J.
PA Loyola University of Chicago, USA; The American National Red Cross
SO U.S., 81 pp., Cont.-in-part of U.S. Ser. No. 351,006, abandoned.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K038-36
NCL 514002000; 514021000; 623011000
CC 63-7 (Pharmaceuticals)
FAN.CNT 8

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6559119	B1	20030506	US 1995-486048	19950607 <--
	EP 1142581	A2	20011010	EP 2001-113651	19911127 <--
	EP 1142581	A3	20020911		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	AU 9884192	A1	19981105	AU 1998-84192	19980911
	AU 733471	B2	20010517		
PRAI	US 1990-618419	B2	19901127 <--		
	US 1991-798919	B2	19911127 <--		
	US 1993-31164	B1	19930312		
	US 1994-328552	B2	19941025		
	US 1994-351006	B2	19941207		
	EP 1992-901268	A3	19911127 <--		
	AU 1994-63648	A3	19940314		

AB This invention provides methods for the preparation of a tissue sealant-treated biomaterial, wherein the tissue sealant used in the method comprises at least one composition which is selected from one or more antibodies, analgesics, anticoagulants, anti-inflammatory compds., antimicrobial compns., antiproliferatives, cytokines, cytotoxins, drugs, growth factors, interferons, hormones, lipids, demineralized bone or bone morphogenetic proteins, cartilage inducing factors, oligonucleotides **polymers**, polysaccharides, polypeptides, protease inhibitors, vasoconstrictors or vasodilators, vitamins, minerals, stabilizers and the like. Further provided are the biomaterial prepared therefrom, including vascular grafts.

ST blood vessel graft tissue sealant biomedical device
IT Heart
Hip
(artificial; method of preparing a tissue sealant-treated biomedical material)
IT Medical goods
(bags; method of preparing a tissue sealant-treated biomedical material)
IT Drug delivery systems
(carriers; method of preparing a tissue sealant-treated biomedical material)
IT **Medical goods**
(**catheters**; method of preparing a tissue sealant-treated biomedical material)
IT Medical goods
(dressings; method of preparing a tissue sealant-treated biomedical material)
IT Drug delivery systems
(emulsions; method of preparing a tissue sealant-treated biomedical material)
IT Drug delivery systems
(films; method of preparing a tissue sealant-treated biomedical material)
IT Cartilage

(formation; method of preparing a tissue sealant-treated biomedical material)
IT Collagens, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(growth factors; method of preparing a tissue sealant-treated biomedical material)
IT **Prosthetic materials and Prosthetics**
(**implants, vascular**; method of preparing a tissue sealant-treated biomedical material)
IT Dental materials and appliances
Drug delivery systems
Prosthetic materials and Prosthetics
(**implants**; method of preparing a tissue sealant-treated biomedical material)
IT Cartilage
(inducing factors; method of preparing a tissue sealant-treated biomedical material)
IT Joint, anatomical
(knee, artificial; method of preparing a tissue sealant-treated biomedical material)
IT Eye
(lens, artificial; method of preparing a tissue sealant-treated biomedical material)
IT Antibiotics
Antitumor agents
Antiviral agents
Bone formation
Cell migration
Cell proliferation
Contact lenses
Drugs
Human
Medical equipment
Sealing compositions
(method of preparing a tissue sealant-treated biomedical material)
IT Antibodies
Fibrinogens
Fibrins
Fluoropolymers, biological studies
Growth factors, animal
Oligonucleotides
Platelet-derived growth factors
Polysaccharides, biological studies
Transforming growth factors
Vitamins
RL: TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of preparing a tissue sealant-treated biomedical material)
IT Growth factors, animal
RL: TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(osteogenins; method of preparing a tissue sealant-treated biomedical material)
IT Medical goods
(sponges; method of preparing a tissue sealant-treated biomedical material)
IT Drug delivery systems
(**sustained-release**; method of preparing a tissue sealant-treated biomedical material)
IT Heart
(valve; method of preparing a tissue sealant-treated biomedical material)
IT 106096-92-8P, Hbgf-1
RL: BPN (Biosynthetic preparation); PUR (Purification or recovery); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method of preparing a tissue sealant-treated biomedical material)
IT 127464-60-2, Vascular endothelial growth factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(method of preparing a tissue sealant-treated biomedical material)
IT 60-01-5, Tributyrin **33069-62-4, Taxol**
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(method of preparing a tissue sealant-treated biomedical material)
IT 7440-70-2, Calcium, biological studies 9002-04-4, Thrombin 9002-84-0, Polytetrafluoroethylene 9013-56-3, Blood coagulation factor xiii 61912-98-9, Igf 62031-54-3, Fgf 62229-50-9, Egf
RL: TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of preparing a tissue sealant-treated biomedical material)
RE.CNT 292 THERE ARE 292 CITED REFERENCES AVAILABLE FOR THIS RECORD
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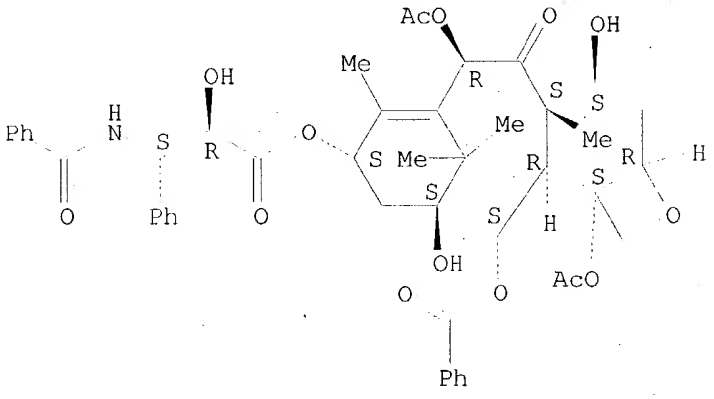
IT **33069-62-4, Taxol**
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(method of preparing a tissue sealant-treated biomedical material)
RN 33069-62-4 HCAPLUS
CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L60 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **2003:92410** HCAPLUS
DN **138:131119**
ED Entered STN: 06 Feb 2003
TI **Vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**
IN **Kunz, Lawrence L.; Klein, Richard A.**
PA NeoRx Corporation, USA
SO U.S., 61 pp., Cont.-in-part of U.S. 5,811,447.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K031-40
NCL 514411000; 514499000; 514319000; 514324000; 514422000; 514428000
CC 1-8 (Pharmacology)
Section cross-reference(s): 28, 63
FAN.CNT 14

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6515009	B1	20030204	US 1995-389712	19950215 <--
	WO 9407529	A1	19940414	WO 1992-US8220	19920925 <--
	W: CA, JP, US				

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    EP 1350523        A2   20031008       EP 2003-15404    19920925 <--
    EP 1350523        A3   20031210
        R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, IE
    US 5811447        A    19980922       US 1995-450793   19950525
    US 6171609        B1   20010109       US 1995-546794   19951023
    CA 2212537        AA   19960822       CA 1996-2212537  19960215
    WO 9625176        A1   19960822       WO 1996-US2125   19960215
        W:  AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE,
            ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT,
            LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
            SG, SI
        RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE,
            IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE
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    EP 809515         A1   19971203       EP 1996-906490   19960215
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            IE, SI, LT, LV
    JP 11500635       T2   19990119       JP 1996-525163   19960215
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    US 6358989        B1   20020319       US 1999-361194   19990726
    US 2002025979     A1   20020228       US 2001-896208   20010629
    US 2002040064     A1   20020404       US 2001-910387   20010720 <--
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    US 6663881        B2   20031216
PRAI US 1991-767254   A2   19910927  <--
    WO 1992-US8220    A2   19920925  <--
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    US 1995-450793    A2   19950525
    EP 1994-911762    A3   19920925  <--
    US 1995-389712    A3   19950215
    WO 1996-US2125    W    19960215
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    US 1997-829991    A3   19970331
    US 1999-361194    A1   19990726
    US 2001-896208    A1   20010629
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AB Methods are provided for inhibiting stenosis following **vascular** trauma or disease in a mammalian host, comprising administering to the host a therapeutically effective dosage of a therapeutic conjugate containing a **vascular smooth muscle** binding protein that assocs. in a specific manner with a **cell** surface of the **vascular smooth muscle cell,** coupled to a therapeutic agent dosage form that inhibits a cellular activity of the **muscle cell.** Methods are also provided for the direct and/or targeted delivery of therapeutic agents to **vascular smooth muscle cells** that cause a dilation and fixation of the **vascular** lumen by inhibiting **smooth muscle cell** contraction, thereby constituting a biol. **stent.** Preparation and testing of roridin A-monoclonal antibody conjugates are described.

ST stenosis inhibition **vascular smooth muscle** binding protein drug conjugate; monoclonal antibody roridin A conjugate prepn stenosis inhibition; targeted drug conjugate **vascular smooth muscle** therapeutic biol **stent**

IT Animal **cell** line
(A375; **vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

IT Animal **cell** line
(B054; **vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)
IT DNA formation
(DNA synthesis inhibition; **vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)
IT Immunoglobulins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(G2b, monoclonal; **vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)
IT Animal **cell** line
(M14; **vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)
IT Toxins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(and toxin subunits; **vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)
IT **Artery**
(**angioplasty; vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)
IT Artery
(arteromyectomy; **vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)
IT Peptides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(binding; **vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)
IT **Medical goods**
(**catheters; vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)
IT Proteoglycans, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(chondroitin sulfate-containing; **vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)
IT Cytotoxic agents
(conjugates with proteins or peptides; **vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)
IT Peptides, biological studies
Proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(conjugates, with cytocidal agents; **vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

IT Cytoskeleton
(cytoskeletal inhibitor; **vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

IT Organelle
(elastic fiber, epitope; **vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

IT Collagens, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(epitope; **vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

IT Glycoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(extracellular, epitope; **vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydroxycarboxylic acid-based; **vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

IT Drug delivery systems
(infusions; **vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

IT Animal tissue
(interstitial, interstitial matrix; **vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

IT Particles
(latex; **vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

IT Proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ligand-binding; **vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

IT **Blood vessel**
(luminal area; **vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

IT Drug delivery systems
(microparticles; **vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

IT Antibodies

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal, NR-AN-01; **vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

IT Drug delivery systems
(nanoparticles; **vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

IT Aggregation
(particle; **vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

IT Latex
(particles; **vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

IT Polymers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polymeric matrix-containing dosage form; **vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

IT Lactones
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polymers; **vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

IT Translation, genetic
(protein synthesis inhibition; **vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

IT **Artery, disease**
(**restenosis; vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

IT Animal **cell**
(reticulum epitope; **vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

IT **Blood vessel**
(**smooth muscle, cell**, migration and contraction; **vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

IT **Artery, disease**
(**stenosis; vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

IT Animal **cell**
(stromal **cell; vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

IT Drug delivery systems

(sustained-release; **vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

IT Artery, disease
(trauma; **vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

IT Cardiovascular agents
Cytotoxic agents
Drug targets
Human
Lysosome
Phagocytosis
(**vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

IT **Cell migration**
(**vascular smooth muscle** cell; **vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

IT **Blood vessel, disease**
(**vascular** trauma; **vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

IT 14729-29-4, Roridin A
RL: PAC (Pharmacological activity); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(**vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

IT 155656-23-8DP, monoclonal antibody conjugates 155656-25-0DP, monoclonal antibody conjugates
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

IT 55-63-0, Nitroglycerin 145-63-1, Suramin 14930-96-2, Cytochalasin B 14930-96-2D, Cytochalasin B, analogs 22144-76-9, Cytochalasin C 22144-77-0, Cytochalasin D 37187-49-8, Cytochalasin 37187-49-8D, Cytochalasin, analogs 62996-74-1, Staurosporin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

IT 108-24-7, Acetic anhydride 108-30-5, Succinic anhydride, reactions 6066-82-6, N-Hydroxysuccinimide 18162-48-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(**vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

IT 154024-51-8P 154024-55-2P 154024-56-3P 155656-22-7P 155656-23-8P 155656-24-9P 155656-25-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(**vascular smooth muscle** binding protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

IT 26009-03-0, Polyglycolide 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26202-08-4, Polyglycolide 26680-10-4, Polylactide 26780-50-7, Poly(lactide-co-glycolide)
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**vascular smooth muscle** binding
protein-therapeutic agent conjugate for therapeutic inhibitor of **vascular smooth muscle cells**)

RE.CNT 381 THERE ARE 381 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L60 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **2002:688475** HCAPLUS
DN **137:222053**
ED Entered STN: 11 Sep 2002
TI **Sustained release** hydrophobic bioactive PLGA microspheres
IN Vook, Noelle Christine; Jacob, Elliott; Setterstrom, Jean A.; Van Hamont, John; Vaughan, William; Duong, Ha
PA United States Dept. of the Army, USA
SO U.S., 40 pp., Cont.-in-part of U.S. 6,309,669.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61F013-00
ICS A61F002-00; A61K009-32; A61K009-22
NCL 424422000
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
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AB A **controlled-release** microcapsulate pharmaceutical formulation for burst-free, **sustained**, programmable **release** of hydrophobic bioactive agent over a duration from 24 h to 100 days comprises a blend of end-capped and uncapped biocompatible, biodegradable poly(lactide/glycolide). For example, **paclitaxel** (**taxol**) was used as a prototype hydrophobic drug for the development of a PLGA copolymer delivery vehicle. **Paclitaxel** was efficiently encapsulated in PLGA using solvent evaporation methodol. The structural stability of RG502 (non-H and H)-containing **paclitaxel** microspheres was optimal with the copolymer blend methodol. As the concentration of RG504, high mol. weight copolymer, increased, the size of the microsphere increased. This relationship held true for H series and non-H series copolymers. As the concentration of RG502 (non-H and H) increased, the **paclitaxel release** rate increased. In comparing **paclitaxel release** rates at the end of the **release** period, **paclitaxel** formulations containing the H-series copolymers **released paclitaxel** at a rate 3-10 times greater than those containing the non-H series copolymers; therefore, the H-series copolymers significantly increased **paclitaxel release** rates. The size of the microsphere was affected by the mol. weight of the copolymer, with predominantly H-series containing **paclitaxel** formulations having the smallest microspheres. Smaller microspheres which contained a higher percentage of RG502 (non-H and H) exhibited **paclitaxel release** rates faster than larger microspheres which contained a higher percentage of RG504 (non-H and H).

ST polylactide polyglycolide encapsulation **controlled sustained** drug **release**; microcapsule **controlled sustained release** polylactide polyglycolide

IT Antibodies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor; **controlled-release** hydrophobic bioactive poly(lactide-glycolide) microspheres for hydrophobic drugs)

IT Intestine, neoplasm
(colorectal, inhibitors; **controlled-release** hydrophobic bioactive poly(lactide-glycolide) microspheres for hydrophobic drugs)

IT Radiation
(combination with; **controlled-release** hydrophobic bioactive poly(lactide-glycolide) microspheres for hydrophobic drugs)

IT Angiogenesis inhibitors
Anti-inflammatory agents
Antibiotics
Antitumor agents
Antiviral agents
Chemotherapy
Dissolution
Particle size distribution
Radiosensitizers, biological
(**controlled-release** hydrophobic bioactive poly(lactide-glycolide) microspheres for hydrophobic drugs)

IT Cytokines
Polymer blends
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**controlled-release** hydrophobic bioactive poly(lactide-glycolide) microspheres for hydrophobic drugs)

IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(dilactone-based; **controlled-release** hydrophobic bioactive poly(lactide-glycolide) microspheres for hydrophobic drugs)
IT Drug delivery systems
(immunotoxins; **controlled-release** hydrophobic bioactive poly(lactide-glycolide) microspheres for hydrophobic drugs)
IT **Drug delivery systems**
(**implants, controlled-release;** **controlled-release** hydrophobic bioactive poly(lactide-glycolide) microspheres for hydrophobic drugs)
IT Drug delivery systems
(infusions; **controlled-release** hydrophobic bioactive poly(lactide-glycolide) microspheres for hydrophobic drugs)
IT Brain, neoplasm
Edema
Esophagus, neoplasm
Kidney, neoplasm
Liver, neoplasm
Lung, neoplasm
Mammary gland, neoplasm
Melanoma
Ovary, neoplasm
Pancreas, neoplasm
Prostate gland, neoplasm
(inhibitors; **controlled-release** hydrophobic bioactive poly(lactide-glycolide) microspheres for hydrophobic drugs)
IT Drug delivery systems
(injections, i.m.; **controlled-release** hydrophobic bioactive poly(lactide-glycolide) microspheres for hydrophobic drugs)
IT Drug delivery systems
(injections, s.c.; **controlled-release** hydrophobic bioactive poly(lactide-glycolide) microspheres for hydrophobic drugs)
IT Drug delivery systems
(microcapsules, **sustained-release;** **sustained-release** hydrophobic bioactive pol(lactide-glycolide) microspheres for hydrophobic drugs)
IT Encapsulation
(microencapsulation; **controlled-release** hydrophobic bioactive poly(lactide-glycolide) microspheres for hydrophobic drugs)
IT Drug delivery systems
(microspheres, **controlled-release;** **controlled-release** hydrophobic bioactive poly(lactide-glycolide) microspheres for hydrophobic drugs)
IT **33069-62-4, Paclitaxel**
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**controlled-release** hydrophobic bioactive poly(lactide-glycolide) microspheres for hydrophobic drugs)
IT 26780-50-7, Glycolide-lactide copolymer 34346-01-5, Resomer RG 502
RL: POF (Polymer in formulation); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**controlled-release** hydrophobic bioactive poly(lactide-glycolide) microspheres for hydrophobic drugs)
IT 51-21-8, 5-Fluorouracil 443-48-1, Metronidazole 7689-03-4, Camptothecin 15663-27-1, Cisplatin 23214-92-8, Doxorubicin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**controlled-release** hydrophobic bioactive poly(lactide-glycolide) microspheres for hydrophobic drugs)
IT 57-50-1, Sucrose, uses
RL: MOA (Modifier or additive use); USES (Uses)
(drug **release** in presence of; **controlled-release** hydrophobic bioactive poly(lactide-glycolide) microspheres for hydrophobic drugs)
RE.CNT 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD

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(41) Tice; US 4542025 A 1985 HCAPLUS
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(44) Tice; US 4835139 A 1989 HCAPLUS
(45) Tice; US 4897268 A 1990
(46) Tice; US 5075109 A 1991 HCAPLUS
(47) Tice; US 5360610 A 1994 HCAPLUS
(48) Tice; US 5407609 A 1995
(49) Tice; US 5811128 A 1998 HCAPLUS
(50) Tice; US 5814344 A 1998 HCAPLUS
(51) Tice; US 5820883 A 1998 HCAPLUS
(52) Tice; US 5853763 A 1998 HCAPLUS

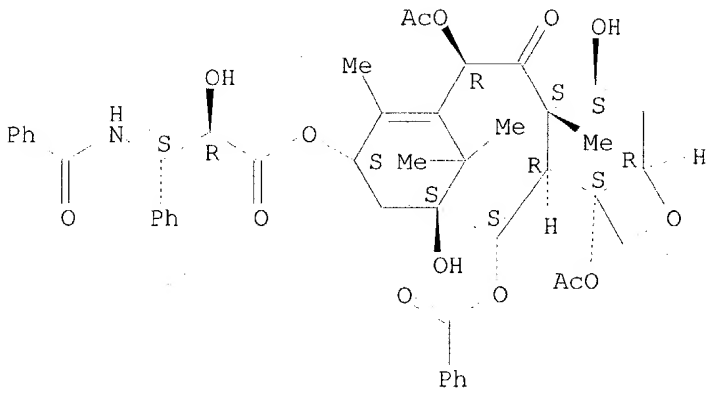
IT **33069-62-4, Paclitaxel**
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**controlled-release** hydrophobic bioactive poly(lactide-glycolide) microspheres for hydrophobic drugs)

RN 33069-62-4 HCAPLUS

CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl

ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L60 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:718980 HCAPLUS
DN 131:327502
ED Entered STN: 11 Nov 1999
TI Therapeutic inhibitor of **vascular smooth muscle cells**
IN **Kunz, Lawrence L.; Klein, Richard A.; Reno, John M.**
PA NeoRx Corporation, USA
SO U.S., 74 pp., Cont.-in-part of U.S. 5,811,447.
CODEN: USXXAM
DT Patent
LA English
IC A61K031-40
NCL 514411000
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 26
FAN.CNT 14

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI US 5981568	A	19991109	US 1997-829685	19970331	
EP 1350523	A2	20031008	EP 2003-15404	19920925	<--
EP 1350523	A3	20031210			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, IE					
US 6515009	B1	20030204	US 1995-389712	19950215	<--
US 5811447	A	19980922	US 1995-450793	19950525	
WO 9625176	A1	19960822	WO 1996-US2125	19960215	
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI					
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE					
WO 9843618	A2	19981008	WO 1998-US6322	19980331	
WO 9843618	A3	19981105			
W: BR, CA, JP					
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
EP 975340	A2	20000202	EP 1998-914366	19980331	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
BR 9808109	A	20000308	BR 1998-8109	19980331	
JP 2001521503	T2	20011106	JP 1998-541922	19980331	

	US 6358989	B1	20020319	US 1999-361194	19990726
	US 2002086896	A1	20020704	US 2001-24885	20011218
	US 6663881	B2	20031216		
	US 2003203958	A1	20031030	US 2002-330834	20021227
PRAI	US 1993-62451	B1	19930513		
	US 1995-389712	A2	19950215		
	US 1995-450793	A2	19950525		
	WO 1996-US2125	A2	19960215		
	US 1991-767254	A2	19910927	<--	
	EP 1994-911762	A3	19920925	<--	
	WO 1992-US8220	A2	19920925	<--	
	US 1993-11669	B2	19930128		
	US 1997-829685	A	19970331		
	US 1997-829991	A	19970331		
	WO 1998-US6322	W	19980331		
	US 1999-361194	A1	19990726		
	US 2001-24885	A1	20011218		

AB Methods are provided for inhibiting stenosis or **restenosis** following vascular trauma in a mammalian host, comprising administering to the host a therapeutically effective dosage of a cytostatic agent and/or cytoskeletal inhibitor so as to biol. **stent** the traumatized vessel. Also provided is a method to inhibit or reduce vascular remodeling following vascular trauma, comprising administering an effective amount of a cytoskeletal inhibitor. Further provided are pharmaceutical compns. and kits comprising the therapeutic agents of the invention.

ST **vascular smooth muscle** regeneration inhibitor stenosis

IT Drug delivery systems
(adventitial wraps; antistenosis inhibitor of **vascular smooth muscle** regeneration)

IT **Artery**
(**angioplasty**, trauma from; antistenosis inhibitor of **vascular smooth muscle** regeneration)

IT **Biodegradable** materials
Blood vessel
Cytotoxic agents
(antistenosis inhibitor of **vascular smooth muscle** regeneration)

IT **Medical goods**
(**catheters**; antistenosis inhibitor of **vascular smooth muscle** regeneration)

IT Artery
(coronary; antistenosis inhibitor of **vascular smooth muscle** regeneration)

IT Drug delivery systems
(gels; antistenosis inhibitor of **vascular smooth muscle** regeneration)

IT Drug delivery systems
(immunotoxins; antistenosis inhibitor of **vascular smooth muscle** regeneration)

IT **Drug delivery systems**
(**implants**; antistenosis inhibitor of **vascular smooth muscle** regeneration)

IT Cytoskeleton
(inhibitors; antistenosis inhibitor of **vascular smooth muscle** regeneration)

IT Drug delivery systems
(membranes; antistenosis inhibitor of **vascular smooth muscle** regeneration)

IT Drug delivery systems
(microparticles; antistenosis inhibitor of **vascular smooth muscle** regeneration)

IT Antibodies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(monoclonal, conjugates; antistenosis inhibitor of **vascular smooth muscle** regeneration)

IT Drug delivery systems
(nanoparticles; antistenosis inhibitor of **vascular smooth muscle** regeneration)

IT Drug delivery systems
(pastes; antistenosis inhibitor of **vascular smooth muscle** regeneration)

IT Proliferation inhibition
(proliferation inhibitors; antistenosis inhibitor of **vascular smooth muscle** regeneration)

IT Medical goods
(shunts; antistenosis inhibitor of **vascular smooth muscle** regeneration)

IT **Artery, disease**
(**stenosis**; antistenosis inhibitor of **vascular smooth muscle** regeneration)

IT **Medical goods**
(**stents**; antistenosis inhibitor of **vascular smooth muscle** regeneration)

IT Crystals
(**sustained-release** dosage forms; antistenosis inhibitor of **vascular smooth muscle** regeneration)

IT Drug delivery systems
(**sustained-release**; antistenosis inhibitor of **vascular smooth muscle** regeneration)

IT **Blood vessel**
(trauma; antistenosis inhibitor of **vascular smooth muscle** regeneration)

IT Drug delivery systems
Transplant and Transplantation
(**vascular**; antistenosis inhibitor of **vascular smooth muscle** regeneration)

IT 14110-64-6, Cytochalasin A 14930-96-2, Cytochalasin b **33069-62-4**, **Taxol** 37187-49-8, Cytochalasin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(antistenosis inhibitor of **vascular smooth muscle** regeneration)

IT 14729-29-4DP, Roridin A, conjugates 51724-48-2DP, Trichothecene, conjugates
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antistenosis inhibitor of **vascular smooth muscle** regeneration)

IT 62996-74-1, Staurosporin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antistenosis inhibitor of **vascular smooth muscle** regeneration)

IT 108-30-5, reactions 6066-82-6, N-Hydroxysuccinimide 14729-29-4, Roridin A 18162-48-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(antistenosis inhibitor of **vascular smooth muscle** regeneration)

IT 154024-51-8P 154024-55-2P 154024-56-3P 155656-22-7P 155656-23-8P
155656-24-9P 155656-25-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(antistenosis inhibitor of **vascular smooth muscle** regeneration)

RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD

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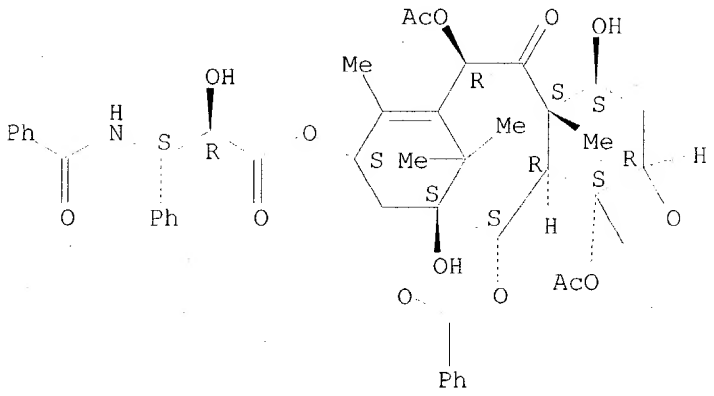
IT **33069-62-4, Taxol**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(antistenosis inhibitor of **vascular smooth muscle** regeneration)

RN 33069-62-4 HCAPLUS

CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L60 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1998:682102 HCAPLUS

DN 129:285998

ED Entered STN: 28 Oct 1998

TI Therapeutic cytostatic and/or cytoskeletal inhibitor for **vascular smooth muscle cells**

IN **Kunz, Lawrence L.; Klein, Richard A.; Reno, John M.**

PA Neorx Corp., USA

SO PCT Int. Appl., 174 pp.
CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K031-00

CC 1-8 (Pharmacology)
Section cross-reference(s): 63

FAN.CNT 14

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9843618	A2	19981008	WO 1998-US6322	19980331
WO 9843618	A3	19981105		
W: BR, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1350523	A2	20031008	EP 2003-15404	19920925 <--
EP 1350523	A3	20031210		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, IE				
US 5981568	A	19991109	US 1997-829685	19970331
EP 975340	A2	20000202	EP 1998-914366	19980331
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9808109	A	20000308	BR 1998-8109	19980331
JP 2001521503	T2	20011106	JP 1998-541922	19980331

PRAI US 1997-829685 A 19970331
US 1997-829991 A 19970331
EP 1994-911762 A3 19920925 <--
US 1993-62451 B1 19930513
US 1995-389712 A2 19950215
US 1995-450793 A2 19950525
WO 1996-US2125 A2 19960215
WO 1998-US6322 W 19980331

AB Methods are provided for inhibiting stenosis or **restenosis** following vascular trauma in a mammalian host, comprising administering to the host a therapeutically effective dosage of a cytostatic agent and/or cytoskeletal inhibitor so as to biol. **stent** the traumatized vessel. Also provided is a method to inhibit or reduce vascular remodeling following vascular trauma, comprising administering an effective amount of a cytoskeletal inhibitor. Further provided are pharmaceutical compns. and kits comprising the therapeutic agents of the invention.

ST **vascular smooth muscle** therapeutic cytoskeletal inhibitor; cytostatic **vascular smooth muscle** therapeutic; stenosis **restenosis** cytostatic cytoskeletal inhibitor; trauma **vascular** biol **stent** cytoskeletal inhibitor

IT **Artery**
(**angioplasty**; therapeutic cytostatic and/or cytoskeletal inhibitor for **vascular smooth muscle cells**)

IT **Medical goods**
(**catheters**; therapeutic cytostatic and/or cytoskeletal inhibitor for **vascular smooth muscle cells**)

IT Artery, disease
(coronary, trauma; therapeutic cytostatic and/or cytoskeletal inhibitor for **vascular smooth muscle cells**)

IT Drug delivery systems
(crystals and microcrystals; therapeutic cytostatic and/or cytoskeletal inhibitor for **vascular smooth muscle cells**)

IT Metabolism
(cytochalasin B; therapeutic cytostatic and/or cytoskeletal inhibitor for **vascular smooth muscle cells**)

IT Toxins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(exotoxins, Pseudomonas, and monoclonal antibody conjugates; therapeutic cytostatic and/or cytoskeletal inhibitor for **vascular smooth muscle cells**)

IT Drug delivery systems
(gels; therapeutic cytostatic and/or cytoskeletal inhibitor for **vascular smooth muscle cells**)

IT **Drug delivery systems**
(**implants**; therapeutic cytostatic and/or cytoskeletal inhibitor for **vascular smooth muscle cells**)

IT Particles
(latex; therapeutic cytostatic and/or cytoskeletal inhibitor for **vascular smooth muscle cells**)

IT Drug delivery systems
(liqs.; therapeutic cytostatic and/or cytoskeletal inhibitor for **vascular smooth muscle cells**)

IT Membranes, nonbiological
(matrix; therapeutic cytostatic and/or cytoskeletal inhibitor for

vascular smooth muscle cells)
IT Drug delivery systems
(microparticles; therapeutic cytostatic and/or cytoskeletal inhibitor for **vascular smooth muscle cells**
)
IT Antibodies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(monoclonal, NR-AN-01; therapeutic cytostatic and/or cytoskeletal inhibitor for **vascular smooth muscle cells**)
IT Antibodies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(monoclonal, conjugates, with derivatized Roridin A; therapeutic cytostatic and/or cytoskeletal inhibitor for **vascular smooth muscle cells**)
IT Drug delivery systems
(nanoparticles; therapeutic cytostatic and/or cytoskeletal inhibitor for **vascular smooth muscle cells**
)
IT Latex
(particles; therapeutic cytostatic and/or cytoskeletal inhibitor for **vascular smooth muscle cells**)
IT Drug delivery systems
(pastes; therapeutic cytostatic and/or cytoskeletal inhibitor for **vascular smooth muscle cells**)
IT Proliferation inhibition
(proliferation inhibitors; therapeutic cytostatic and/or cytoskeletal inhibitor for **vascular smooth muscle cells**)
IT **Blood vessel**
(remodeling; therapeutic cytostatic and/or cytoskeletal inhibitor for **vascular smooth muscle cells**)
IT **Artery, disease**
(**restenosis**; therapeutic cytostatic and/or cytoskeletal inhibitor for **vascular smooth muscle cells**)
IT **Blood vessel**
(**smooth muscle**; therapeutic cytostatic and/or cytoskeletal inhibitor for **vascular smooth muscle cells**)
IT **Artery, disease**
(**stenosis**; therapeutic cytostatic and/or cytoskeletal inhibitor for **vascular smooth muscle cells**)
IT **Medical goods**
(**stents**, biol. stenting; therapeutic cytostatic and/or cytoskeletal inhibitor for **vascular smooth muscle cells**)
IT Drug delivery systems
(**sustained-release**; therapeutic cytostatic and/or cytoskeletal inhibitor for **vascular smooth muscle cells**)
IT **Cell migration**
Cytoskeleton
Cytotoxic agents
(therapeutic cytostatic and/or cytoskeletal inhibitor for **vascular smooth muscle cells**)
IT Artery, disease
Blood vessel, disease
(trauma; therapeutic cytostatic and/or cytoskeletal inhibitor for

vascular smooth muscle cells)

IT Drug delivery systems
(unit doses; therapeutic cytostatic and/or cytoskeletal inhibitor for **vascular smooth muscle cells**)

IT 154024-51-8P 154024-55-2P 154024-56-3P 155656-22-7P 155656-23-8P 155656-24-9P 155656-25-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction; therapeutic cytostatic and/or cytoskeletal inhibitor for **vascular smooth muscle cells**)

IT 14729-29-4, Roridin A
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(reaction; therapeutic cytostatic and/or cytoskeletal inhibitor for **vascular smooth muscle cells**)

IT 108-24-7, Acetic anhydride 108-30-5, Succinic anhydride, reactions 18162-48-6, tert-Butyldimethylsilyl chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; therapeutic cytostatic and/or cytoskeletal inhibitor for **vascular smooth muscle cells**)

IT 55-63-0, Nitroglycerin 145-63-1, Suramin 62996-74-1, Staurosporin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(therapeutic cytostatic and/or cytoskeletal inhibitor for **vascular smooth muscle cells**)

IT 155656-23-8DP, monoclonal antibody reaction products 155656-25-0DP, monoclonal antibody reaction products
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(therapeutic cytostatic and/or cytoskeletal inhibitor for **vascular smooth muscle cells**)

IT 14110-64-6, Cytochalasin A 14930-96-2, Cytochalasin B 14930-96-2D, Cytochalasin B, analogs 22144-76-9, Cytochalasin C 22144-77-0, Cytochalasin D **33069-62-4, Taxol 33069-62-4D**
, **Taxol**, analogs 37187-49-8, Cytochalasin 37187-49-8D, Cytochalasin, analogs
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic cytostatic and/or cytoskeletal inhibitor for **vascular smooth muscle cells**)

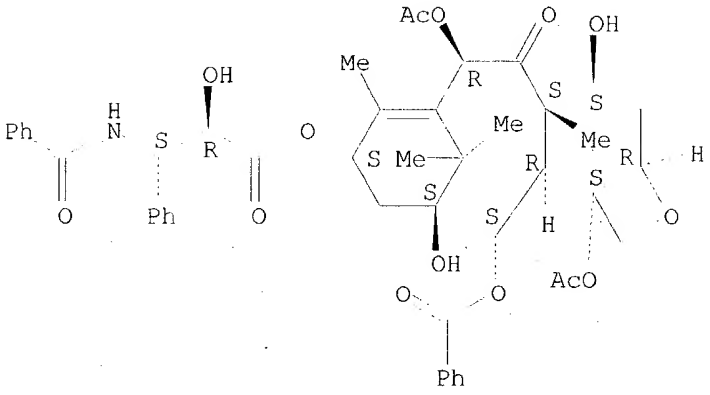
IT 14729-29-4D, Roridin A, derivs., monoclonal antibody conjugates
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(therapeutic cytostatic and/or cytoskeletal inhibitor for **vascular smooth muscle cells**)

IT **33069-62-4, Taxol 33069-62-4D, Taxol**
, analogs
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic cytostatic and/or cytoskeletal inhibitor for **vascular smooth muscle cells**)

RN 33069-62-4 HCAPLUS

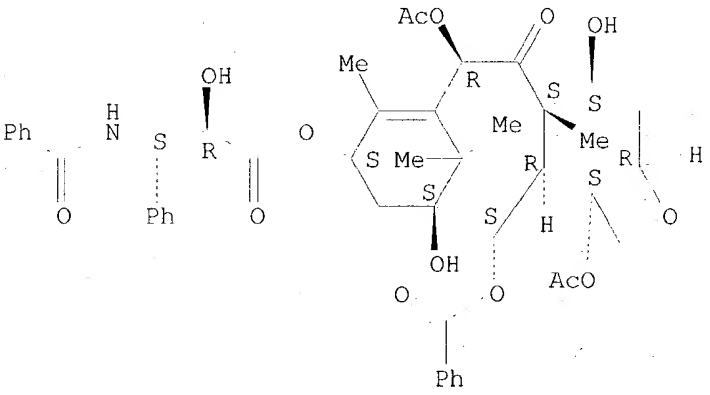
CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 33069-62-4 HCAPLUS
CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L60 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:635115 HCAPLUS
DN 125:266018
ED Entered STN: 28 Oct 1996
TI **Vascular smooth muscle cell** binding protein-therapeutic agent conjugates, and preparation thereof, for therapeutic inhibitors of **vascular smooth muscle cells**
IN **Kunz, Lawrence L.; Reno, John M.**
PA Neorx Corporation, USA
SO PCT Int. Appl., 140 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K047-48
ICS A61K009-00
CC 1-8 (Pharmacology)
Section cross-reference(s): 63
FAN.CNT 14

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE	
PI	WO 9625176	A1	19960822		WO 1996-US2125	19960215	
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI						
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE						
	EP 1350523	A2	20031008		EP 2003-15404	19920925	<--
	EP 1350523	A3	20031210				
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, IE						
	US 6515009	B1	20030204		US 1995-389712	19950215	<--
	AU 9649851	A1	19960904		AU 1996-49851	19960215	
	EP 809515	A1	19971203		EP 1996-906490	19960215	
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV						
	JP 11500635	T2	19990119		JP 1996-525163	19960215	
	US 5981568	A	19991109		US 1997-829685	19970331	
	US 6358989	B1	20020319		US 1999-361194	19990726	
	US 2002025979	A1	20020228		US 2001-896208	20010629	
	US 2003039675	A1	20030227		US 2001-995490	20011127	
	US 6569441	B2	20030527				
	US 2002086896	A1	20020704		US 2001-24885	20011218	
	US 6663881	B2	20031216				
	US 2003083733	A1	20030501		US 2002-190211	20020703	
PRAI	US 1995-389712	A	19950215				
	US 1991-767254	A2	19910927	<--			
	EP 1994-911762	A3	19920925	<--			
	WO 1992-US8220	A2	19920925	<--			
	US 1993-11669	B2	19930128				
	US 1993-62451	A1	19930513				
	US 1995-450793	A2	19950525				
	WO 1996-US2125	W	19960215				
	US 1997-829685	A3	19970331				
	US 1997-829991	A3	19970331				
	US 1997-894350	B1	19971010				
	US 1999-361194	A1	19990726				
	US 2001-896208	A1	20010629				

AB Methods are provided for inhibiting stenosis following **vascular** trauma or disease in mammalian host, comprising administering to the host a therapeutically effective dosage of a therapeutic conjugate containing a **vascular smooth muscle** binding protein that assocs. in a specific manner with a **cell** surface of the **vascular smooth muscle cell**, coupled to a therapeutic agent dosage form that inhibits a cellular activity of the **muscle cell**. Methods are also provided for the direct and/or targeted delivery of therapeutic agents to **vascular smooth muscle cells** that cause a dilatation and fixation of the **vascular** lumen by inhibiting **smooth muscle cell** contraction, thereby constituting a biol. **stent**.

ST **vascular smooth muscle cell** therapeutic conjugate; biol **stent** therapeutic **vascular smooth muscle**

IT Artery
(balloon-traumatized; **vascular smooth muscle cell** binding protein-therapeutic agent conjugates, and preparation thereof, for therapeutic inhibitor of **vascular smooth muscle cells**)

IT Peptides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(binding; **vascular smooth muscle**

cell binding protein-therapeutic agent conjugates, and preparation thereof, for therapeutic inhibitor of **vascular smooth muscle cells**)

IT Cytoskeleton
(inhibitors; **vascular smooth muscle cell** binding protein-therapeutic agent conjugates, and preparation thereof, for therapeutic inhibitor of **vascular smooth muscle cells**)

IT Particles
(latex, monoclonal antibody-conjugated; **vascular smooth muscle cell** binding protein-therapeutic agent conjugates, and preparation thereof, for therapeutic inhibitor of **vascular smooth muscle cells**)

IT Latex
(particles, monoclonal antibody-conjugated; **vascular smooth muscle cell** binding protein-therapeutic agent conjugates, and preparation thereof, for therapeutic inhibitor of **vascular smooth muscle cells**)

IT **Cell** proliferation
(**smooth muscle**, inhibitor; **vascular smooth muscle cell** binding protein-therapeutic agent conjugates, and preparation thereof, for therapeutic inhibitor of **vascular smooth muscle cells**)

IT Metals, biological studies
Plastics
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**stent** of; **vascular smooth muscle cell** binding protein-therapeutic agent conjugates, and preparation thereof, for therapeutic inhibitor of **vascular smooth muscle cells**)

IT Deoxyribonucleic acid formation
Translation, genetic
(**vascular smooth muscle cell** binding protein-therapeutic agent conjugates, and preparation thereof, for therapeutic inhibitor of **vascular smooth muscle cells**)

IT **Artery**
(**angioplasty, vascular smooth muscle cell** binding protein-therapeutic agent conjugates, and preparation thereof, for therapeutic inhibitor of **vascular smooth muscle cells**)

IT Coating materials
(**biodegradable**, for **stent; vascular smooth muscle cell** binding protein-therapeutic agent conjugates, and preparation thereof, for therapeutic inhibitor of **vascular smooth muscle cells**)

IT **Muscle**
(interstitium, **vascular smooth muscle cell** binding protein-therapeutic agent conjugates, and preparation thereof, for therapeutic inhibitor of **vascular smooth muscle cells**)

IT Proteins, specific or class, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ligand-binding, **vascular smooth muscle cell** binding protein-therapeutic agent conjugates, and preparation thereof, for therapeutic inhibitor of **vascular smooth muscle cells**)

IT Antibodies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(monoclonal, NR-AN-01, conjugates with Roridin A; **vascular smooth muscle cell** binding protein-therapeutic agent conjugates, and preparation thereof, for therapeutic inhibitor of **vascular smooth muscle cells**)

IT **Artery, disease**
(**restenosis, vascular smooth muscle cell** binding protein-therapeutic agent conjugates, and preparation thereof, for therapeutic inhibitor of **vascular smooth muscle cells**)

IT **Muscle**
(**smooth, cell, proliferation inhibitor; vascular smooth muscle cell** binding protein-therapeutic agent conjugates, and preparation thereof, for therapeutic inhibitor of **vascular smooth muscle cells**)

IT **Artery, disease**
(**stenosis, vascular smooth muscle cell** binding protein-therapeutic agent conjugates, and preparation thereof, for therapeutic inhibitor of **vascular smooth muscle cells**)

IT **Medical goods**
(**stents**, biol.; **vascular smooth muscle cell** binding protein-therapeutic agent conjugates, and preparation thereof, for therapeutic inhibitor of **vascular smooth muscle cells**)

IT **Muscle**
(stroma, **vascular smooth muscle cell** binding protein-therapeutic agent conjugates, and preparation thereof, for therapeutic inhibitor of **vascular smooth muscle cells**)

IT Pharmaceutical dosage forms
(**sustained-release, vascular smooth muscle cell** binding protein-therapeutic agent conjugates, and preparation thereof, for therapeutic inhibitor of **vascular smooth muscle cells**)

IT **Blood vessel**
(transplant, **vascular smooth muscle cell** binding protein-therapeutic agent conjugates, and preparation thereof, for therapeutic inhibitor of **vascular smooth muscle cells**)

IT **Blood vessel, disease**
(trauma, **vascular smooth muscle cell** binding protein-therapeutic agent conjugates, and preparation thereof, for therapeutic inhibitor of **vascular smooth muscle cells**)

IT 154024-51-8P 154024-55-2P 154024-56-3P 155656-22-7P 155656-23-8P 155656-24-9P 155656-25-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction; **vascular smooth muscle cell** binding protein-therapeutic agent conjugates, and preparation thereof, for therapeutic inhibitor of **vascular smooth muscle cells**)

IT 108-24-7, Acetic anhydride 108-30-5, Succinic anhydride, reactions 6066-82-6, N-Hydroxysuccinimide 14729-29-4, Roridin A 18162-48-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; **vascular smooth muscle cell** binding protein-therapeutic agent conjugates, and preparation thereof, for therapeutic inhibitor of **vascular smooth**

muscle cells)

IT 14729-29-4DP, Roridin A, monoclonal antibody conjugates 155656-23-8DP, monoclonal antibody conjugates 155656-25-0DP, monoclonal antibody conjugates
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**vascular smooth muscle cell** binding protein-therapeutic agent conjugates, and preparation thereof, for therapeutic inhibitor of **vascular smooth muscle cells**)

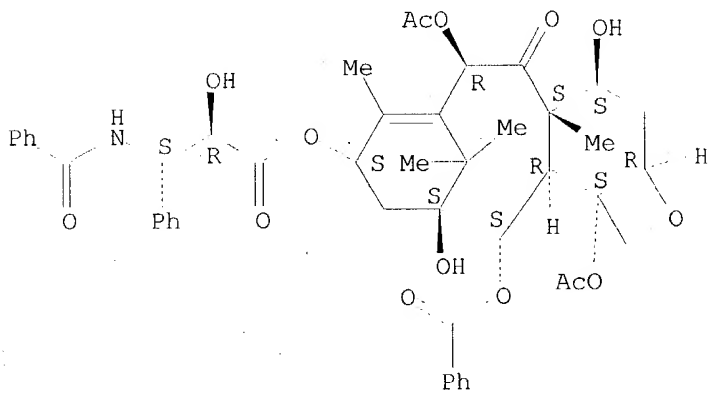
IT 145-63-1, Suramin 14930-96-2, Cytochalasin B 22144-76-9, Cytochalasin C 22144-77-0, Cytochalasin D 37187-49-8, Cytochalasin 62996-74-1, Staurosporin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**vascular smooth muscle cell** binding protein-therapeutic agent conjugates, and preparation thereof, for therapeutic inhibitor of **vascular smooth muscle cells**)

IT 14930-96-2D, Cytochalasin B, analogs **33069-62-4, Taxol** **33069-62-4D, Taxol**, analogs
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**vascular smooth muscle cell** binding protein-therapeutic agent conjugates, and preparation thereof, for therapeutic inhibitor of **vascular smooth muscle cells**)

IT **33069-62-4, Taxol** **33069-62-4D, Taxol**, analogs
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**vascular smooth muscle cell** binding protein-therapeutic agent conjugates, and preparation thereof, for therapeutic inhibitor of **vascular smooth muscle cells**)

RN 33069-62-4 HCAPLUS
CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

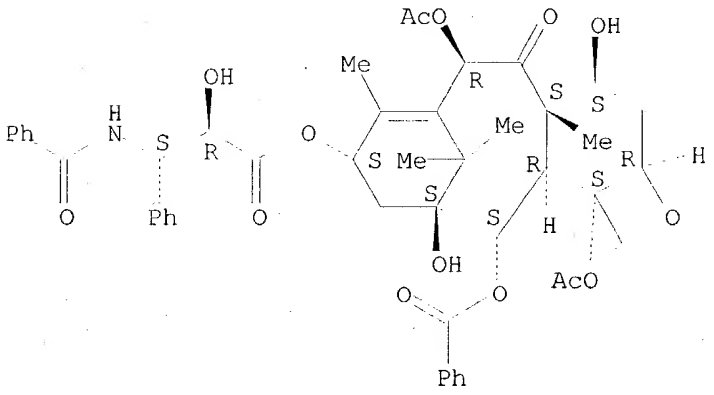
Absolute stereochemistry. Rotation (-).



RN 33069-62-4 HCAPLUS
CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-

2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



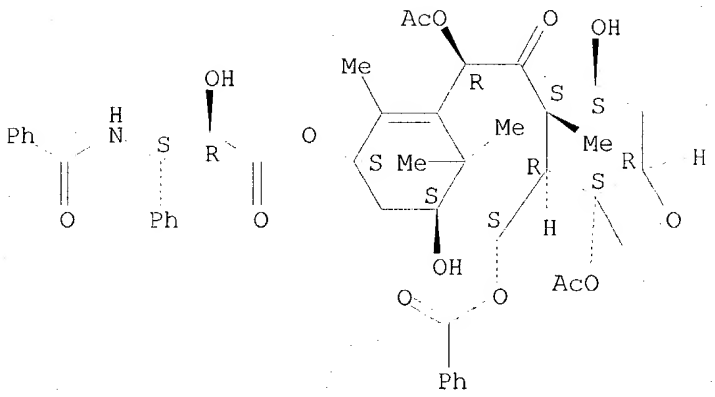
L60 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1994:144136** HCAPLUS
DN **120:144136**
ED Entered STN: 19 Mar 1994
TI Water-soluble polymeric carriers for drug delivery
IN Desai, Neil P.; Soon-Shiong, Patrick; Sandford, Paul A.
PA Clover Consolidated, Ltd., Switz.
SO PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D305-14
CC 63-5 (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9324476	A1	19931209	WO 1993-US5344	19930604 <--
	W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9344067	A1	19931230	AU 1993-44067	19930604 <--
	US 5648506	A	19970715	US 1995-464270	19950605 <--
PRAI	US 1992-893500		19920604 <--		
	WO 1993-US5344		19930604		

AB Polymeric drug delivery systems in which the drug, e.g. **taxol** (I), is bound to a water-soluble polymer, e.g. PEG, to provide a form of soluble drug delivery especially for those cases in which the drug by itself is water-insol are disclosed. I in CHCl3 was mixed with 1,1,-carbonyldiimidazole (II) to obtain I-II derivative which was separated and reacted with monomethoxy polyethylene glycol amine to obtain I-PEG derivative Cross-linked insol. gels of these materials are also prepared to serve as a form of implantable drug delivery.
ST drug delivery system polymer soly; **taxol** PEG deriv drug delivery
IT Pharmaceutical dosage forms
(implants, **sustained-release** drug-polymer conjugates in, preparation of)

IT Pharmaceutical dosage forms
(**sustained-release**, drug-polymer conjugates in, preparation of)
IT 108644-38-8P
RL: RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(preparation and coupling of, with **taxol**)
IT 153177-13-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrolysis of)
IT 32171-39-4P
RL: RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(preparation and polymerization of)
IT 153177-17-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with PEG)
IT 153177-16-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with PEG deriv)
IT 117527-50-1P 117527-51-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with PEG derivative)
IT 31961-02-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with **taxol**)
IT 26403-58-7DP, conjugates with succinyl **taxol** 117527-50-1DP, conjugates with PEG acrylate 153177-11-8P 153177-12-9P 153177-14-1P 153177-15-2P
RL: PREP (Preparation)
(preparation of, for **sustained-release** drug delivery system)
IT 79-10-7, Acrylic acid, biological studies 814-68-6, Acryloyl chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with PEG-acrylate derivative)
IT **33069-62-4, Taxol**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with carbonyldiimidazole)
IT 108-30-5, Succinic anhydride, biological studies
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with monomethoxy polyethylene glycol)
IT 9004-74-4, Monomethoxy polyethylene glycol
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with succinic anhydride)
IT 530-62-1 17341-93-4, 2,2,2-Trichloroethyl chloroformate
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with **taxol**)
IT 80506-64-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with **taxol** derivative)
IT **33069-62-4, Taxol**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with carbonyldiimidazole)
RN 33069-62-4 HCAPLUS
CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L60 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2004 ACS on STN
AN **1993:656526** HCAPLUS
DN **119:256526**
ED Entered STN: 11 Dec 1993
TI Compounds, compositions, and methods for binding bioaffecting substances to surface membranes of bioparticles
IN Kopia, Gregory A.; Horan, Paul K.; Gray, Brian D.; Troutner, David E.; Muirhead, Katharine A.; Lin, Chia En; Sheth, Kamleshkumar A.; Yu, Zhizhou; Lever, Susan Z.; et al.
PA Zynaxis Technologies, Inc., USA
SO PCT Int. Appl., 163 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D263-62
ICS C07D293-00; C07D277-62; C07D209-02; C07D209-04; C07K017-02; C08B037-10; A61K043-00; A61K047-48
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 27
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9311120	A1	19930610	WO 1992-US10076	19921124 <--
	W: AT, AU, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KR, LU, NL, NO, RU, SE				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2051373	AA	19901102	CA 1990-2051373	19900427 <--
	WO 9014435	A1	19901129	WO 1990-US2341	19900427 <--
	W: AU, CA, FI, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
	AU 9056755	A1	19901218	AU 1990-56755	19900427 <--
	AU 645014	B2	19940106		
	EP 471792	A1	19920226	EP 1990-908868	19900427 <--
	EP 471792	B1	19981223		
	R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
	JP 04506113	T2	19921022	JP 1990-508139	19900427 <--
	AT 175025	E	19990115	AT 1990-908868	19900427 <--
	US 5667764	A	19970916	US 1992-884432	19920515 <--
	AU 9332219	A1	19930628	AU 1993-32219	19921124 <--
	EP 643706	A1	19950322	EP 1993-900600	19921124 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, IE, IT, LI, LU, NL, SE				
	JP 08502719	T2	19960326	JP 1993-510190	19921124 <--
	ZA 9209179	A	19930524	ZA 1992-9179	19921126 <--
PRAI	US 1991-798936	A	19911127 <--		

US 1992-884432	A	19920515	<--
US 1988-189192	B2	19880502	<--
US 1989-345436	A	19890501	<--
WO 1990-US2341	A	19900427	<--
WO 1992-US10076	A	19921124	<--

OS MARPAT 119:256526

AB Compds. are provided having the capability of binding therapeutically active substances to lipid-containing biocompatible particles, such as cells or viruses. These compds. include a bioaffecting moiety, comprising a therapeutically active substance, which is linked via a linking moiety to ≥1 hydrocarbon substituent selected so that the compound is sufficiently nonpolar to impart lipid binding capability to the compound Thus, compds. of the invention are useful for site-selective delivery of therapeutic agents, and retention thereof at the selected site. Methods are provided for using various compds. of the invention in treatment of diseases or other pathol. conditions. For example, methods are provided for treatment of postangioplasty **restenosis**, rheumatoid arthritis, tumor cell proliferation, particularly tumor cells associated with ovarian cancer, and psoriasis. Anticoagulant-lipophilic cyanine conjugate (I) exhibited good membrane retention on rabbit red blood cell ghosts. The membrane-bound I retained potent antithrombin activity.

ST drug hydrocarbon conjugate lipid binding; **angioplasty** **restenosis** drug hydrocarbon conjugate; rheumatoid arthritis drug hydrocarbon conjugate; neoplasm inhibitor hydrocarbon conjugate; psoriasis drug hydrocarbon conjugate

IT Tubulins
RL: BIOL (Biological study)
(antiproliferative agent interfering with processes of, conjugates with hydrocarbon compound, for binding to lipid-containing bioparticles)

IT Blood vessel
(antiproliferative drug-hydrocarbon compound conjugate binding to, for reduction of postangioplasty **restenosis**)

IT Synovial membrane
(antiproliferative drug-hydrocarbon compound conjugate binding to, of arthritic joint, for treating rheumatoid arthritis)

IT Particles
(bio-, lipid-containing, therapeutics-hydrocarbon conjugates for binding to)

IT Lipids, biological studies
RL: BIOL (Biological study)
(bioparticles containing, therapeutics-hydrocarbon conjugates for binding to)

IT Anticoagulants and Antithrombotics
Neoplasm inhibitors
Therapeutics
(conjugates with hydrocarbon compound, for binding to lipid-containing bioparticles)

IT Hydrocarbons, compounds
RL: BIOL (Biological study)
(conjugates, with therapeutics, for binding to lipid-containing bioparticles)

IT Cell membrane
(drug-hydrocarbon compound conjugates binding by, of erythrocytes)

IT Blood platelet
Erythrocyte
Leukocyte
(lipid-binding therapeutics-hydrocarbon compound conjugates bound to membrane of, as pharmaceutical delivery vehicle)

IT Lipoproteins
RL: BIOL (Biological study)
(lipid-binding therapeutics-hydrocarbon compound conjugates bound to, as pharmaceutical delivery vehicle)

IT Molecular structure-biological activity relationship

(membrane-binding stability, of drug-hydrocarbon compound conjugates)
IT Halogens
RL: BIOL (Biological study)
(radioactive, therapeutic agent-hydrocarbon compound conjugate containing, for binding to lipid-containing bioparticles)
IT Vasodilators
(substance P-lipophilic cyanine conjugate as)
IT Chelating agents
(therapeutic radionuclide complexes, conjugates with hydrocarbon compound, for binding to lipid-containing bioparticles)
IT Pharmaceutical dosage forms
(therapeutics-hydrocarbon conjugates binding to lipid-containing bioparticles)
IT Psoriasis
(treatment of, antiproliferative drug-hydrocarbon compound conjugate binding to cells of psoriatic lesion for)
IT Polycarbonates, biological studies
Rubber, silicone, biological studies
RL: BIOL (Biological study)
(tubing of, docosanyl-tetradecyl-iodo-tetramethylindocarbocyanine chloride retention on)
IT Diagnosis
(agents, therapeutic agent-hydrocarbon compound conjugate containing, for in vivo detection)
IT **Artery**
(**angioplasty, restenosis** after, prevention of, antiproliferative drug-hydrocarbon compound conjugate binding to blood vessel for)
IT Inflammation inhibitors
(antirheumatics, antiproliferative drug-hydrocarbon compound conjugate binding to synovial membrane of arthritic joint as)
IT Therapeutics
(chemo-, conjugates with hydrocarbon compound, for binding to lipid-containing bioparticles)
IT Radioelements, compounds
RL: BIOL (Biological study)
(complexes, with chelating agent, conjugates with hydrocarbon compound, for binding to lipid-containing bioparticles)
IT Proteins, specific or class
RL: BIOL (Biological study)
(conjugates, with avidin, complexes with biotinylated hydrocarbon compound)
IT Antibodies
Antigens
Enzymes
Hormones
Toxins
RL: BIOL (Biological study)
(conjugates, with hydrocarbon compound, for binding to lipid-containing bioparticles)
IT Avidins
RL: BIOL (Biological study)
(conjugates, with protein, complexes with biotinylated hydrocarbon compound)
IT Ovary, neoplasm
(inhibitors, antiproliferative drug-hydrocarbon compound conjugate binding to tumor cells as)
IT Neoplasm inhibitors
(ovary, antiproliferative drug-hydrocarbon compound conjugate binding to tumor cells as)
IT Heart, disease
(**restenosis**, postangioplasty, prevention of, antiproliferative drug-hydrocarbon compound conjugate binding to blood

vessel for)
IT Alkaloids, compounds
RL: BIOL (Biological study)
(vincaleukoblastine, conjugates, with hydrocarbon compound, for binding to lipid-containing bioparticles)
IT 149980-66-5 149980-67-6
RL: BIOL (Biological study)
(drug delivery by conjugation with hydrocarbon compound and binding to lipid-containing bioparticle in relation to)
IT 58-85-5D, Biotin, conjugates with hydrocarbon compound
RL: BIOL (Biological study)
(for binding avidin-protein complexes)
IT 64-86-8D, Colchicine, conjugates with hydrocarbon compound 8001-27-2D, Hirudin, conjugates with hydrocarbon compound 9005-49-6D, Heparin, conjugates with hydrocarbon compound **33069-62-4D, Taxol**, conjugates with hydrocarbon compound 149980-62-1D, halides 149980-63-2D, halides 149980-64-3D, halides 149980-65-4D, halides
RL: BIOL (Biological study)
(for binding to lipid-containing bioparticles)
IT 70365-31-0 145687-07-6
RL: PRP (Properties)
(membrane binding stability and membrane retention coefficient of)
IT 15105-87-0 68006-78-0 75664-02-7 149959-63-7 149959-64-8 149959-65-9 149959-66-0 149959-67-1 149959-68-2 149959-69-3 149959-71-7
RL: BIOL (Biological study)
(membrane binding stability of)
IT 149959-70-6P
RL: PREP (Preparation)
(membrane binding stability of and preparation and reaction of, in preparation of lipid-binding drug conjugate)
IT 53290-46-3 75664-00-5 129180-49-0 129499-00-9 129499-01-0 129499-02-1 129499-04-3 129499-05-4 129499-06-5 129499-07-6 129499-08-7 149959-62-6
RL: PRP (Properties)
(membrane retention coefficient of)
IT 149959-85-3P
RL: PREP (Preparation)
(preparation and acid cleavability and antiproliferative activity of)
IT 149959-88-6DP, reaction products with heparin
RL: PREP (Preparation)
(preparation and anticoagulant activity and membrane retention of)
IT 151306-92-2P
RL: PREP (Preparation)
(preparation and biodistribution and in vivo retention of)
IT 13116-27-3P, 4-Iodophenylhydrazine 54136-25-3P 129524-46-5P 149959-72-8P 149959-73-9P 149959-74-0P 149959-75-1P 149959-76-2P 149959-77-3P 149959-78-4P 149959-79-5P 149959-82-0P 149959-83-1P 149959-84-2P 149959-86-4P 149959-87-5P 149959-89-7P 149959-91-1P 149980-68-7P 149980-70-1P 149980-71-2P 149980-72-3P 149980-73-4P 150749-61-4P 150749-63-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of lipid-binding drug conjugate)
IT 150749-59-0P
RL: PREP (Preparation)
(preparation of and red blood cell membrane binding by and and vasodilator activity of)
IT 149959-80-8P 149959-81-9P 149959-90-0P
RL: PREP (Preparation)
(preparation of, for binding drug to lipid-containing bioparticles)

IT 95-21-6, 2-Methylbenzoxazole 108-55-4, Glutaric anhydride 118-29-6, N-Hydroxymethylphthalimide 540-37-4, 4-Iodoaniline 563-80-4 1501-27-5 1640-39-7 3476-50-4, Deacetyl colchicine 4538-56-1, N,N-Diphenylformamidine 9005-49-6, Heparin, reactions 33507-63-0, Substance P 33755-53-2, (+)-Biotin 4-nitrophenyl ester 70967-79-2 73206-47-0 89889-52-1 129499-16-7 131270-55-8 149980-69-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of lipid-binding drug conjugate)

IT 1333-74-0D, Hydrogen, radioactive 7440-44-0D, Carbon, radioactive 7704-34-9D, Sulfur, radioactive 7727-37-9D, Nitrogen, radioactive 7782-49-2D, Selenium, radioactive
RL: BIOL (Biological study)
(therapeutic agent-hydrocarbon compound conjugate containing, for binding to lipid-containing bioparticles)

IT 7439-94-3D, Lutetium, chelates, conjugates with hydrocarbon compound 7440-05-3D, Palladium, chelates, conjugates with hydrocarbon compound 7440-15-5D, Rhenium, chelates, conjugates with hydrocarbon compound 7440-16-6D, Rhodium, chelates, conjugates with hydrocarbon compound 7440-19-9D, Samarium, chelates, conjugates with hydrocarbon compound 7440-26-8D, Technetium, chelates, conjugates with hydrocarbon compound 7440-50-8D, Copper, chelates, conjugates with hydrocarbon compound 7440-52-0D, Erbium, chelates, conjugates with hydrocarbon compound 7440-54-2D, Gadolinium, chelates, conjugates with hydrocarbon compound 7440-57-5D, Gold, chelates, conjugates with hydrocarbon compound 7440-60-0D, Holmium, chelates, conjugates with hydrocarbon compound 7440-64-4D, Ytterbium, chelates, conjugates with hydrocarbon compound 7440-65-5D, Yttrium, chelates, conjugates with hydrocarbon compound 7440-74-6D, Indium, chelates, conjugates with hydrocarbon compound
RL: BIOL (Biological study)
(therapeutic, for binding to lipid-containing bioparticles)

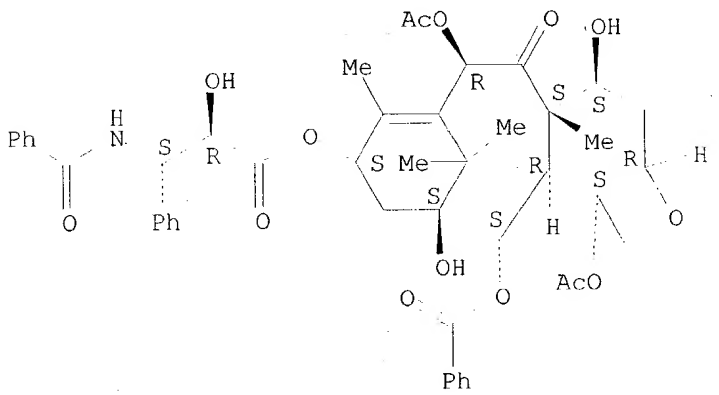
IT 9002-86-2, Polyvinylchloride 9002-88-4, Polyethylene
RL: BIOL (Biological study)
(tubing of, docosanyl-tetradecyl-iodo-tetramethylindocarbocyanine chloride retention on)

IT **33069-62-4D, Taxol**, conjugates with hydrocarbon compound
RL: BIOL (Biological study)
(for binding to lipid-containing bioparticles)

RN 33069-62-4 HCAPLUS

CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



=> => d all

L63 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:400902 HCAPLUS
DN 121:902
ED Entered STN: 09 Jul 1994
TI Therapeutic-binding protein conjugate for inhibitor of **vascular smooth muscle cells**
IN **Kunz, Lawrence Leroy**
PA Neorx Corp., USA
SO PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K039-00
CC 1-8 (Pharmacology)
Section cross-reference(s): 63
FAN.CNT 14

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9407529	A1	19940414	WO 1992-US8220	19920925	
	W: CA, JP, US					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE					
	EP 752885	A1	19970115	EP 1994-911762	19920925	
	EP 752885	B1	20030709			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE					
	AT 244576	E	20030715	AT 1994-911762	19920925	
	EP 1350523	A2	20031008	EP 2003-15404	19920925	
	EP 1350523	A3	20031210			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, IE					
	US 6515009	B1	20030204	US 1995-389712	19950215	
	US 6251920	B1	20010626	US 1998-82643	19980521	
	US 6262079	B1	20010717	US 1999-306606	19990506	
	US 6268390	B1	20010731	US 1999-470662	19991222	
	US 2002013275	A1	20020131	US 2001-910388	20010720	<--
	US 2002040064	A1	20020404	US 2001-910387	20010720	
	US 6599928	B2	20030729			
PRAI	US 1991-767254	A2	19910927			
	EP 1994-911762	A3	19920925			
	WO 1992-US8220	W	19920925			
	US 1993-11669	B2	19930128			
	US 1993-61714	B2	19930513			
	US 1993-62451	A1	19930513			
	US 1994-241844	B2	19940512			
	US 1994-242161	A2	19940512			
	US 1995-389712	A1	19950215			
	US 1995-450793	A2	19950525			
	US 1995-486334	A3	19950607			
	US 1998-82643	A1	19980521			
	US 1998-113733	A1	19980710			
	US 1999-470662	A1	19991222			

AB Methods are provided for inhibiting stenosis following **vascular** trauma or disease in a mammalian host, comprising administering to the host a therapeutically effective dosage of a therapeutic conjugate containing a **vascular smooth muscle** binding protein that assocs. in a specific manner with a **cell** surface of the **vascular smooth muscle cell**, coupled to a therapeutic agent that inhibits a cellular activity of the **muscle cell**. Preparation and testing of Roridin A-monoclonal antibody conjugates is described.

ST **vascular smooth muscle cell** inhibitor conjugate; binding protein therapeutic conjugate **smooth**

muscle; Roridin monoclonal antibody conjugate **smooth muscle**

IT Collagens, biological studies
RL: BIOL (Biological study)
(binding proteins specific for, conjugates with therapeutics, for noncytocidal **vascular smooth muscle cell** inhibition)

IT Therapeutics
(conjugates, with binding proteins specific for **vascular smooth muscle cells**, for noncytocidal **cell** inhibition)

IT Pseudomonas
(exotoxin of, binding protein conjugates, for cancer treatment)

IT Glycoproteins, biological studies
RL: BIOL (Biological study)
(extracellular, binding proteins specific for, conjugates with therapeutics, for noncytocidal **vascular smooth muscle cell** inhibition)

IT Particles
(gold, **vascular smooth muscle cell**-specific monoclonal antibody coated on, binding and internalization by **vascular smooth muscle cells** of)

IT Deoxyribonucleic acid formation
(inhibition of, of **vascular smooth muscle cell**, therapeutic conjugates with binding proteins specific for **vascular smooth muscle cell** for)

IT Neoplasm inhibitors
(therapeutic-binding protein conjugates for)

IT **Artery**
(**angioplasty, restenosis** following, treatment of, therapeutic conjugates with binding proteins specific for **vascular smooth muscle cells** for)

IT Peptides, biological studies
Proteins, specific or class
RL: BIOL (Biological study)
(conjugates, **vascular smooth muscle cell**-specific, with therapeutics, for noncytocidal **cell** inhibition)

IT Immunity
(disorder, treatment of, therapeutic-binding protein conjugate for)

IT Toxins
RL: BIOL (Biological study)
(exo-, Pseudomonas, binding protein conjugates, for cancer treatment)

IT Antibodies
RL: BIOL (Biological study)
(monoclonal, **vascular smooth muscle cell**-specific, conjugates with Roridin A, for noncytocidal **cell** inhibition)

IT Heart, disease
(**restenosis**, post-**angioplasty**, treatment of, therapeutic conjugates with binding proteins specific for **vascular smooth muscle cells** for)

IT **Muscle**
(**smooth, vascular**, binding proteins specific for **cell** of, conjugates with therapeutics, for noncytocidal **cell** inhibition)

IT **Muscle**
(stroma, binding proteins specific for **cell** of, conjugates with therapeutics, for noncytocidal **vascular smooth muscle cell** inhibition)

IT Pharmaceutical dosage forms
(sustained-release, of therapeutic conjugates with binding proteins

specific for **vascular smooth muscle cells**, for noncytocidal **cell** inhibition)
IT 14729-29-4D, Roridin A, binding protein conjugates
RL: BIOL (Biological study)
(for cancer treatment)
IT 55-63-0D, Nitroglycerin, conjugates with **vascular smooth muscle cell**-specific binding proteins 145-63-1D, Suramin, conjugates with **vascular smooth muscle cell**-specific binding proteins 62996-74-1D, Staurosporin, conjugates with **vascular smooth muscle cell**-specific binding proteins
RL: BIOL (Biological study)
(for noncytocidal **vascular smooth muscle cell** inhibition)
IT 9026-43-1, Protein kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, conjugates with **vascular smooth muscle cell**-specific binding proteins, for noncytocidal **cell** inhibition)
IT 7440-57-5, Gold, biological studies
RL: BIOL (Biological study)
(particles, **vascular smooth muscle cell**-specific monoclonal antibody coated on, binding and internalization by **vascular smooth muscle cells** of)
IT 154024-51-8P 154024-55-2P 154024-56-3P 155656-22-7P 155656-24-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in Roridin A derivative preparation for monoclonal antibody conjugation)
IT 155656-23-8P 155656-25-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of and **vascular smooth muscle cell**-specific monoclonal antibody conjugation of)
IT 9007-28-7, Chondroitin sulfate
RL: BIOL (Biological study)
(proteoglycan, binding proteins specific for, conjugates with therapeutics, for noncytocidal **vascular smooth muscle cell** inhibition)
IT 108-30-5, reactions 18162-48-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with Roridin A)
IT 6066-82-6, N-Hydroxysuccinimide
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with Roridin A hemisuccinic acid)
IT 14729-29-4, Roridin A
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with succinic anhydride and with t-butyldimethylsilyl chloride)

=> => d l61 all hitstr tot

L61 ANSWER 1 OF 30 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:2750 HCAPLUS
DN 140:47582
ED Entered STN: 02 Jan 2004
TI Silicone blends and composites for drug delivery
IN Ratner, Buddy; Kwok, Connie; Walline, Katie; Johnston, Erika; Miller, Robert J.
PA Genzyme Corporation, USA
SO PCT Int. Appl., 38 pp.

CODEN: PIXXD2
DT Patent
LA English
IC ICM A61L027-44
ICS A61L027-48; A61L027-54; A61L029-12; A61L029-16; A61L031-12; A61L031-16
CC 63-6 (Pharmaceuticals)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000382	A1	20031231	WO 2003-US19676	20030620

PI
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-390665P P 20020621

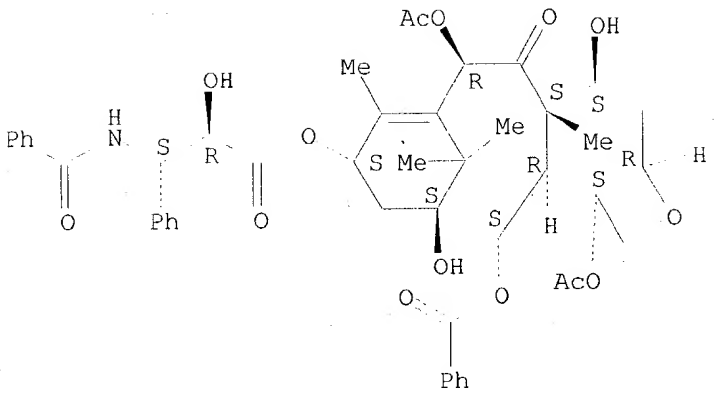
AB The present invention provides a composition for use in delivering a drug into the body of a mammal, wherein the composition comprises silicone elastomer, an adjuvant **polymer**, and the drug. This composition may be part of an implantable medical device, such as a **stent** or a vascular or other graft or sheath, among other configurations. When the compns. are used as coating, the coating may further include a top-coat of silicone or silicone and adjuvant **polymer** mixture For a hydrophilic drug, Tranilast, it was shown that the incorporation of PEG increases the initial burst rate ,while decreasing the subsequent steady state release rate. Release of the drug was not zero order and leveled off to zero after 21 days. Adding a topcoat to the Tranilast/silicone coating somewhat leveled off the initial burst, but did not extend the release past 21 days.

ST drug delivery silicone blend composite
IT Platelet (blood)
(aggregation; silicone blends and composites for drug delivery)
IT **Artery**
(**angioplasty**, devices for; silicone blends and composites for drug delivery)
IT Heart, disease
(arrhythmia; silicone blends and composites for drug delivery)
IT Medical goods
(arterial-venous shunt; silicone blends and composites for drug delivery)
IT Blood vessel
(artificial; silicone blends and composites for drug delivery)
IT Medical goods
(cannulas; silicone blends and composites for drug delivery)
IT Polyesters, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(caprolactone-based; silicone blends and composites for drug delivery)
IT **Medical goods**
(**catheters**; silicone blends and composites for drug delivery)
IT Polyesters, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydroxycarboxylic acid-based; silicone blends and composites for drug delivery)
IT **Prosthetic materials and Prosthetics**
(**implants**, artificial heart pacemaker; silicone blends and

composites for drug delivery)
IT **Drug delivery systems**
(**implants, sustained-release**; silicone blends and composites for drug delivery)
IT **Prosthetic materials and Prosthetics**
(**implants**; silicone blends and composites for drug delivery)
IT Polyesters, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lactic acid-based; silicone blends and composites for drug delivery)
IT Polyethers, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ortho ester group-containing; silicone blends and composites for drug delivery)
IT **Prosthetic materials and Prosthetics**
(orthopedic; silicone blends and composites for drug delivery)
IT Heart
(pacemaker, artificial; silicone blends and composites for drug delivery)
IT Polysulfones, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyether-; silicone blends and composites for drug delivery)
IT Polyethers, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polysulfone-; silicone blends and composites for drug delivery)
IT Anti-inflammatory agents
Antiarrhythmics
Antibiotics
Anticoagulants
Antimicrobial agents
Deformation (mechanical)
Drug delivery systems
Inflammation
Needles (tools)
Platelet aggregation inhibitors
Surfactants
(silicone blends and composites for drug delivery)
IT Carbon fibers, biological studies
Fluoropolymers, biological studies
Polyanhydrides
Polycarbonates, biological studies
Polyesters, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(silicone blends and composites for drug delivery)
IT Antisense DNA
Polyamides, biological studies
Polyamines
Polymers, biological studies
Polyoxyalkylenes, biological studies
Polysaccharides, biological studies
Polyurethanes, biological studies
Silicone rubber, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(silicone blends and composites for drug delivery)
IT **Medical goods**
(**stents**; silicone blends and composites for drug delivery)
IT Medical goods
(sutures; silicone blends and composites for drug delivery)
IT Heart

(valve, artificial; silicone blends and composites for drug delivery)
IT Medical goods
(wire guides; silicone blends and composites for drug delivery)
IT 7439-88-5, Iridium, biological studies 7440-06-4, Platinum, biological studies 7440-22-4, Silver, biological studies 7440-25-7, Tantalum, biological studies 7440-32-6, Titanium, biological studies 7440-33-7, Tungsten, biological studies 7440-44-0, Carbon, biological studies 7440-57-5, Gold, biological studies 9002-84-0, PTFE 9002-88-4, Polyethylene 9003-07-0, Polypropylene 9004-35-7, Cellulose acetate 9004-70-0, Cellulose nitrate 12597-68-1, Stainless steel, biological studies 12606-02-9, Inconel 24980-41-4, Polycaprolactone 25038-59-9, PET, biological studies 25248-42-4, Polycaprolactone 26009-03-0, Poly(glycolic acid) 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26063-00-3, Poly(3-hydroxybutyric acid) 26100-51-6, Polylactic acid 26124-68-5, Poly(glycolic acid) 26744-04-7 34346-01-5, Glycolic acid-lactic acid **copolymer** 52013-44-2, Nitinol 67291-18-3, Poly(3-hydroxyvaleric acid), SRU 83120-66-5, Poly(3-hydroxyvaleric acid)
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(silicone blends and composites for drug delivery)
IT 79-10-7D, Acrylic acid, esters, **polymers** 1951-25-3, Amiodarone 9002-89-5, Poly(vinyl alcohol) 9002-98-6 9003-20-7, Poly(vinyl acetate) 9003-39-8, Polyvinylpyrrolidone 9004-34-6D, Cellulose, derivs. 9004-54-0, Dextran, biological studies 9004-61-9, Hyaluronic acid 9004-61-9D, Hyaluronic acid, derivs. 9005-49-6, Heparin, biological studies 9005-82-7, Polyamylose 9007-28-7, Chondroitin sulfate 24967-94-0, Dermatan sulfate 25189-55-3, Poly(N-isopropylacrylamide) 25322-68-3, Polyethylene glycol **33069-62-4**, **Paclitaxel** 53123-88-9, Rapamycin 53123-88-9D, Rapamycin, derivs. 53902-12-8, Tranilast 68424-04-4, Polydextrose 70226-44-7, Heparan 85721-33-1, Ciprofloxacin 106392-12-5, Pluronic 121749-39-1, DENSPM
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(silicone blends and composites for drug delivery)
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Control Delivery Systems; WO 0236175 A 2002 HCAPLUS
(2) Paco Res Corp; EP 0224981 A 1987 HCAPLUS
(3) Schneider Usa Inc; EP 0923953 A 1999 HCAPLUS
(4) St Petersburg Traumatology Orthopaedics; RU 2103013 C 1998 HCAPLUS
IT **33069-62-4**, **Paclitaxel**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(silicone blends and composites for drug delivery)
RN 33069-62-4 HCAPLUS
CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L61 ANSWER 2 OF 30 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:1007933 HCAPLUS
DN 140:47564
ED Entered STN: 28 Dec 2003
TI Implantable medical devices for controlled delivery of drugs
IN Schwarz, Marlene C.
PA USA
SO U.S. Pat. Appl. Publ., 20 pp.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K009-22
ICS A61F013-00; A61M031-00
NCL 604890100; 604500000
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 37
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003236514	A1	20031225	US 2002-175136	20020619
WO 2004000384	A1	20031231	WO 2003-US19269	20030619

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-175136 A 20020619
AB The present invention is directed to implantable or insertable medical devices that provide **controlled release** of a drug. A drug-**releasing** medical device is provided, which comprises: (a) an implantable or insertable medical device; (b) a **release** layer disposed over at least a portion of the implantable or insertable medical device; and (c) a drug. The **release** layer comprises a maleic anhydride **polymer** selected from (i) a maleic anhydride **copolymer** and (ii) a maleic anhydride graft **polymer**. The **release** layer regulates the rate of **release** of the therapeutic agent from the medical device upon implantation or insertion of the device into a patient. The present invention is also directed to methods of forming the above implantable or insertable medical devices,

methods of administering a therapeutic agent to a patient using such devices, and methods of modulating the **release** of therapeutic agent from such devices. A solution is provided that contains 25THF, 74% toluene, 0.25% **paclitaxel** and 0.75% a **polymer** composition, which consists of a polystyrene-polyisobutylene-polystyrene block **copolymer** (SIBS), a random **copolymer** of styrene and maleic anhydride containing 14-15% maleic anhydride (SMA14), or a blend of these **polymers.** A **stent** is mounted onto a holding device parallel to the nozzle and, if desired, rotated to ensure uniform coverage. After a carrier coating is formed in this fashion, the **stent** is dried, e.g., by placing it in a preheated oven for 30 min at 65°, followed by 3 h at 70°. Three **stents** are formed in this manner for each of the various **polymeric** solns. The **release** rate of a therapeutic agent from a carrier layer comprising a **copolymer** of maleic anhydride and styrene can be modulated by the addition of a blending **polymer** in various proportions.

ST implant medical device **controlled** delivery drug; maleic anhydride **polymer** medical device drug **release**

IT Blood vessel
(artificial; implantable medical devices for controlled delivery of drugs)

IT **Medical goods**
(**catheters**; implantable medical devices for controlled delivery of drugs)

IT Intestine
(colon; implantable medical devices for controlled delivery of drugs)

IT **Artery, disease**
(**coronary, restenosis**; implantable medical devices for controlled delivery of drugs)

IT Artery
(coronary; implantable medical devices for controlled delivery of drugs)

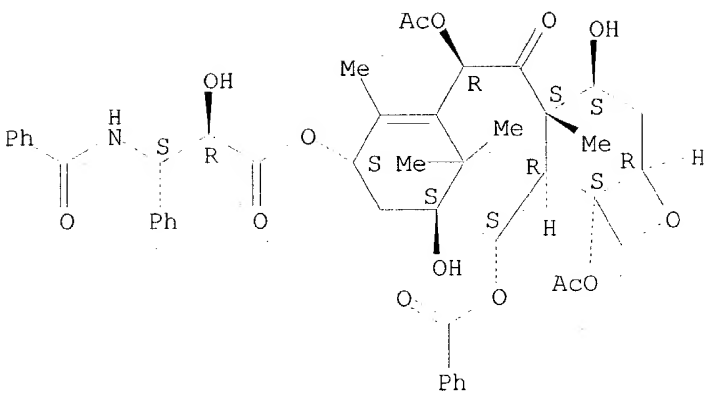
IT Medical goods
(guide wires; implantable medical devices for controlled delivery of drugs)

IT Anesthetics
Anti-inflammatory agents
Anticholesteremic agents
Anticoagulants
Antitumor agents
Biliary tract
Blood vessel
Brain
Cytotoxic agents
Esophagus
Extracellular matrix
Human
Hypercholesterolemia
Medical goods
Mitosis
Molecular weight distribution
Neoplasm
Prostate gland
Solvents
Thrombosis
Trachea (anatomical)
Urinary tract
Vasodilators
(implantable medical devices for controlled delivery of drugs)

IT **Polymer** blends
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(implantable medical devices for controlled delivery of drugs)
IT **Drug delivery systems**
(**implants, controlled-release;**
implantable medical devices for **controlled** delivery of drugs)
IT **Prosthetic materials and Prosthetics**
(**implants;** implantable medical devices for controlled
delivery of drugs)
IT Vinyl compounds, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**polymers;** implantable medical devices for controlled
delivery of drugs)
IT Dissolution
(rate; implantable medical devices for controlled delivery of drugs)
IT **Medical goods**
(**stents;** implantable medical devices for controlled delivery
of drugs)
IT 108-31-6D, Maleic anhydride, **polymers** 9003-27-4,
Polyisobutylene 9003-53-6, Polystyrene 9003-63-8, Poly(butyl methacrylate) 9006-26-2, Ethylene-maleic anhydride **copolymer** 9011-13-6, Maleic anhydride-styrene **copolymer** 9011-16-9, Gantrez AN 25722-45-6 26426-80-2, Isobutylene-maleic anhydride **copolymer** 37324-80-4, Maleic anhydride-styrene **copolymer** methyl ester 52229-50-2, Maleic anhydride-methyl vinyl ether alternating **copolymer** 106209-33-0, Maleic anhydride-styrene alternating **copolymer** 110171-93-2, Isobutylene-maleic anhydride alternating **copolymer** 112020-31-2, Maleic anhydride-styrene graft **copolymer** 382162-07-4, Butylene-ethylene block **copolymer** 636600-64-1
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(implantable medical devices for controlled delivery of drugs)
IT **33069-62-4, Paclitaxel**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(implantable medical devices for controlled delivery of drugs)
IT 109671-82-1, Isobutylene-styrene block **copolymer**
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(triblock; implantable medical devices for controlled delivery of
drugs)
IT **33069-62-4, Paclitaxel**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(implantable medical devices for controlled delivery of drugs)
RN 33069-62-4 HCAPLUS
CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-,
(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L61 ANSWER 3 OF 30 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:1007932 HCAPLUS
DN 140:47563
ED Entered STN: 28 Dec 2003
TI Implantable medical devices for controlled delivery of pharmaceuticals
IN Schwarz, Marlene C.; Richard, Robert E.
PA **Scimed Life Systems, Inc., USA**
SO U.S. Pat. Appl. Publ., 15 pp.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61F013-00
ICS A61K009-22
NCL 604890100; 424426000
CC 63-6 (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003236513	A1	20031225	US 2002-174286	20020619
	WO 2004000381	A1	20031231	WO 2003-US19309	20030619

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-174286 A 20020619

AB The present invention is directed to implantable or insertable medical devices that provide release of a therapeutic agent. According to a first aspect of the present invention, a therapeutic-agent-releasing medical device is provided, which comprises: (a) an implantable or insertable medical device; (b) a release layer disposed over at least a portion of the implantable or insertable medical device, and (c) a therapeutic agent. The release layer regulates the rate of release of the therapeutic agent from the medical device upon implantation or insertion of the device into a patient. The release layer comprises (i) a first **polymer** comprising one or more **polymer** chains that form one or more **polymer** phase domains when the first **polymer** is in a pure solid-state form; and (ii) a second **polymer** comprising two or more **polymer** chains that form two or more phase domains when

the second **polymer** is in a pure solid-state form. The first and second **polymers** are preferably selected such that at least one **polymer** chain in the second **polymer** is compatible with at least one **polymer** chain in the first **polymer**. The present invention is also directed to methods of forming the above implantable or insertable medical devices, methods of administering a therapeutic agent to a patient using such devices, and methods of modulating the release of therapeutic agents from implantable or insertable medical devices. Solns. are provided that contain 99% CHCl3, 0.25% **paclitaxel** and 0.75% a **polymer** composition or blend. One solution is prepared by mixing 0.75% the block **copolymer** polystyrene-polyisobutylene-polystyrene block **copolymer** (SIBS) with the solvent and **paclitaxel**. A second solution is prepared by mixing 0.75% the block **copolymer** polystyrene-polyvinylpyrrolidone (PS/PVP) with the solvent and **paclitaxel**. A third solution is prepared by blending 0.30% the PS/PVP **copolymer** and 0.45% the SIBS **copolymer** with the solvent and **paclitaxel**. All solns. are prepared by (1) mixing the **paclitaxel** and a small amount of the chloroform, (2) adding the **polymer** or **copolymers**, (3) adding the remaining chloroform, (4) thoroughly mixing (e.g., overnight), and (5) filtering. The release rate of a therapeutic agent from a **polymeric** carrier layer can be modulated by changing the ratio of the hydrophilic and hydrophobic **polymeric** components by blending a hydrophobic **polymeric** drug carrier with a block **copolymer** containing at least one hydrophilic **polymer** chain and at least one hydrophilic **polymer** chain.

ST implantable medical device controlled delivery pharmaceutical; **polymer** controlled delivery pharmaceutical medical device; polystyrene block controlled delivery pharmaceutical medical device

IT Blood vessel
(artificial; implantable medical devices for controlled delivery of pharmaceuticals)

IT **Polymers**, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(block; implantable medical devices for controlled delivery of pharmaceuticals)

IT **Medical goods**
(**catheters**; implantable medical devices for controlled delivery of pharmaceuticals)

IT Intestine
(colon; implantable medical devices for controlled delivery of pharmaceuticals)

IT **Artery, disease**
(**coronary, restenosis**; implantable medical devices for controlled delivery of pharmaceuticals)

IT Artery
(coronary; implantable medical devices for controlled delivery of pharmaceuticals)

IT **Polymers**, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(graft; implantable medical devices for controlled delivery of pharmaceuticals)

IT Medical goods
(guide wires; implantable medical devices for controlled delivery of pharmaceuticals)

IT Anesthetics
Anti-inflammatory agents
Anticholesteremic agents
Anticoagulants
Antitumor agents

Biliary tract
Brain
Esophagus
Extracellular matrix
Human
Hypercholesterolemia
Inflammation
Medical goods
Mitosis
Neoplasm
Prostate gland
Spraying
Thrombosis
Trachea (anatomical)
Urinary tract
Vasodilators
(implantable medical devices for controlled delivery of pharmaceuticals)

IT **Polymer** blends
RL: DEV (Device component use); POF (Polymer in formulation); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(implantable medical devices for controlled delivery of pharmaceuticals)

IT **Polymers**, biological studies
Polyolefins
Polyoxyalkylenes, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(implantable medical devices for controlled delivery of pharmaceuticals)

IT **Drug delivery systems**
(**implants**, **controlled-release**; implantable medical devices for **controlled** delivery of pharmaceuticals)

IT **Prosthetic materials and Prosthetics**
(**implants**; implantable medical devices for controlled delivery of pharmaceuticals)

IT Blood vessel
(peripheral; implantable medical devices for controlled delivery of pharmaceuticals)

IT Vinyl compounds, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**polymers**, aromatic; implantable medical devices for controlled delivery of pharmaceuticals)

IT Vinyl compounds, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**polymers**; implantable medical devices for controlled delivery of pharmaceuticals)

IT Dissolution
(rate; implantable medical devices for controlled delivery of pharmaceuticals)

IT **Medical goods**
(**stents**; implantable medical devices for controlled delivery of pharmaceuticals)

IT Aromatic compounds
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vinyl, **polymers**; implantable medical devices for controlled delivery of pharmaceuticals)

IT 108548-52-3, Polyethylene glycol-styrene block **copolymer**
120293-17-6, Acrylic acid-styrene block **copolymer**

RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(di- and triblock; implantable medical devices for controlled delivery of pharmaceuticals)

IT 124400-28-8, Acrylamide-styrene block **copolymer** 151306-42-2, Sodium Acrylate-styrene block **copolymer**
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diblock; implantable medical devices for controlled delivery of pharmaceuticals)

IT 9002-89-5, Poly(vinyl alcohol) 9003-01-4, Polyacrylic acid 9003-05-8, Polyacrylamide 9003-27-4, Polyisobutylene 9003-39-8, Polyvinylpyrrolidone 9003-47-8, Poly(vinylpyridine) 9003-53-6, Polystyrene 24937-72-2, Poly(maleic anhydride) 25087-26-7, **Polymethacrylic** acid 25322-68-3, Polyethylene oxide 26793-34-0, Polydimethylacrylamide 109671-82-1, Isobutylene-styrene block **copolymer** 116219-50-2, Agrimer ST
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(implantable medical devices for controlled delivery of pharmaceuticals)

IT 67-66-3, Chloroform, uses
RL: NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process); USES (Uses)
(implantable medical devices for controlled delivery of pharmaceuticals)

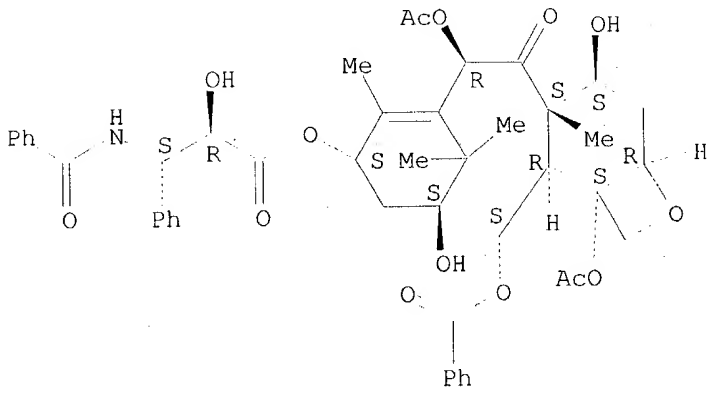
IT **33069-62-4, Paclitaxel**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(implantable medical devices for controlled delivery of pharmaceuticals)

IT **33069-62-4, Paclitaxel**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(implantable medical devices for controlled delivery of pharmaceuticals)

RN 33069-62-4 HCAPLUS

CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L61 ANSWER 4 OF 30 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:614144 HCAPLUS
ED Entered STN: 11 Aug 2003

TI Randomized Study to Assess the Effectiveness of Slow- and Moderate-Release **Polymer**-Based **Paclitaxel**-Eluting **Stents** for Coronary Artery Lesions
AU Colombo, Antonio; Drzewiecki, Janusz; Banning, Adrian; Grube, Eberhard; Hauptmann, Karl; Silber, Sigmund; Dudek, Dariusz; Fort, Stephen; Schiele, Francois; Zmudka, Krysztof; Guagliumi, Giulio; Russell, Mary E.
CS Ospedale San Raffaele, Milan, Italy
SO Circulation (2003), 108(7), 788-794
CODEN: CIRCAZ; ISSN: 0009-7322
PB Lippincott Williams & Wilkins
DT Journal
LA English
CC 63 (Pharmaceuticals)
AB Background- Early clin. studies demonstrated the feasibility of local **paclitaxel** delivery in reducing **restenosis** after treatment of de novo coronary lesions in small patient populations. Methods and Results- We conducted a randomized, double-blind trial of 536 patients at 38 medical centers evaluating slow-**release** (SR) and moderate-**release** (MR) formulations of a **polymer**-based **paclitaxel**-eluting **stent** (TAXUS) for revascularization of single, primary lesions in native coronary arteries. Cohort I compared TAXUS-SR with **control stents**, and Cohort II compared TAXUS-MR with a second **control** group. The primary end point was 6-mo percent in-**stent** net volume obstruction measured by intravascular ultrasound. Secondary end points were 6-mo angiog. **restenosis** and 6- and 12-mo incidence of major adverse cardiac events, a composite of cardiac death, myocardial infarction, and repeat revascularization. At 6 mo, percent net volume obstruction within the **stent** was significantly lower for TAXUS **stents** (7.9% SR and 7.8% MR) than for resp. **controls** (23.2% and 20.5%; P<0.0001 for both). This corresponded with a reduction in angiog. **restenosis** from 17.9% to 2.3% in the SR cohort (P<0.0001) and from 20.2% to 4.7% in the MR cohort (P=0.0002). The incidence of major adverse cardiac events at 12 mo was significantly lower (P=0.0192) in the TAXUS-SR (10.9%) and TAXUS-MR (9.9%) groups than in **controls** (22.0% and 21.4%, resp.), predominantly because of a significant reduction in repeat revascularization of the target lesion in TAXUS-treated patients. Conclusions- Compared with a bare metal **stent**, **paclitaxel**-eluting **stents** reduced in-**stent** neointimal formation and **restenosis** and improved 12-mo clin. outcome of patients with single de novo coronary lesions.
RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Costa, M; Am J Cardiol 2000, V85, P135 MEDLINE
(2) Grube, E; Circulation 2003, V107, P38 HCAPLUS
(3) Hamers, R; Comp Cardiol 2001, V28, P589
(4) Morice, M; N Engl J Med 2002, V346, P1773 HCAPLUS
(5) Park, S; N Engl J Med 2003, V348, P1537 HCAPLUS
(6) Serruys, P; Quantitative Coronary Angiography in Clinical Practice Dordrecht 1994
(7) Silber, S; Handbook of Coronary Stents 4th ed 2001, P311
(8) Sollott, S; J Clin Invest 1995, V95, P1869 HCAPLUS
(9) Sousa, J; Circulation 2003, V107, P2383
(10) Tanabe, K; Circulation 2003, V107, P559
(11) Uretsky, B; Am Heart J 2000, V140, P804 MEDLINE

L61 ANSWER 5 OF 30 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:610313 HCAPLUS
DN 139:138816
ED Entered STN: 08 Aug 2003
TI Medical device for delivering therapeutic materials
IN Rosenthal, Arthur L.; Shaw, William J.
PA **Scimed Life Systems, Inc., USA**

SO PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61L027-00
CC 63-7 (Pharmaceuticals)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003063924	A1	20030807	WO 2003-US2585	20030130

PI
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

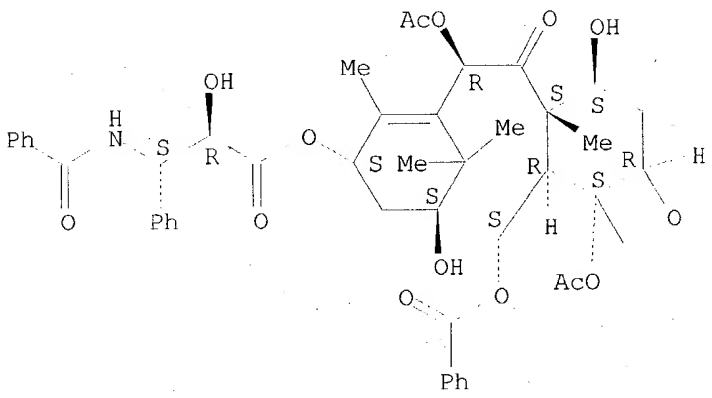
PRAI US 2002-62794 A 20020131

AB A medical device for delivering a therapeutic materials into a body tissue, comprises **struts** and optionally the biol. active material. In an embodiment, the medical device comprises non-structural elements integral with the **struts**. A method for designing such medical device is also disclosed. Another embodiment is a medical device having an outer surface comprising a middle section and end sections. The end sections having a greater available surface area, greater affinity for or a greater amount of the biol. active material per unit length of the outer surface than the middle section. The middle section may be covered with a barrier layer. Another embodiment is a medical device comprising a rectangular portion having a greater capacity for carrying a biol. active material per unit length of the outer surface.

ST medical device therapeutic material
IT Medical goods
(medical device for delivering therapeutic materials)
IT DNA
RNA
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medical device for delivering therapeutic materials)
IT 50-02-2, Dexamethasone 1402-38-6, Actinomycin 10102-43-9D, Nitric oxide, adducts **33069-62-4**, **Paclitaxel** 53123-88-9, Sirolimus 55837-20-2, Halofuginone 104987-11-3, Tacrolimus 159351-69-6, Everolimus
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medical device for delivering therapeutic materials)
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Hossainy; US 6287628 B1 2001 HCAPLUS
(2) Jayaraman; US 6517889 B1 2003 HCAPLUS
(3) Khosravi; US 6458152 B1 2002
(4) New; US 6471979 B2 2002 HCAPLUS
(5) Rudakov; US 6451050 B1 2002
(6) Sass; US 6383215 B1 2002
(7) Sirhan; US 6471980 B2 2002 HCAPLUS
(8) Wright; US 6273913 B1 2001
(9) Yan; US 5843172 A 1998
IT **33069-62-4**, **Paclitaxel**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medical device for delivering therapeutic materials)
RN 33069-62-4 HCAPLUS
CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-,

(2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L61 ANSWER 6 OF 30 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:300921 HCAPLUS
DN 138:309322
ED Entered STN: 18 Apr 2003
TI **Controlled release** drug delivery composition comprising polycationic **polymer** and negatively charged pharmacologically active compound
IN Jackson, John K.; Springate, Chris; Winternitz, Charles; Burt, Helen M.
PA The University of British Columbia, Can.; Arc Pharmaceuticals, Inc.
SO PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K047-34
ICS A61K047-48; A61K048-00
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003030941	A1	20030417	WO 2002-CA1507	20021007
	W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003134810	A1	20030717	US 2002-259260	20020926
PRAI	US 2001-328175P	P	20011009		
	US 2001-328203P	P	20011009		

AB Compns. and methods for in vivo delivery of pharmacol. active agents associated with **polymeric biocompatible** materials are described. Compns. comprise a first, neg. charged pharmacol. active agent, such as an oligonucleotide, and a polycationic **polymer**,

such as chitosan or chitosan derivs., optionally in a pharmaceutically acceptable carrier, providing **controlled release** and/or protection from degradation of the first, neg. charged pharmacol. active agent when introduced into the body. The pharmaceutically acceptable carrier can be a **polymer** paste or gel which may contain a second pharmacol. active agent which may be an anti-inflammatory and/or an anti-proliferative agent. Methods of making and administering a **controlled release** and/or protective from degradation compns. for the delivery of a pharmacol. active agent, such as a nucleic acid, in combination with a polycationic **polymer** and in a pharmaceutically acceptable carrier, to a mammal in a pharmaceutically effective amount For example, 28 mg NaCl and 72 mg chitosan were pulverized and mixed with 36 mg neg. charged. clusterin antisense oligonucleotide to give microparticles. A **polymeric** paste was prepared containing a blend of 600 mg liquid methoxypolyethylene glycol and 400 mg **biodegradable** triblock **polymer** of poly(DL-lactide-co-caprolactone) and polyethylene glycol,. Chitosan/oligonucleotide microparticles (40 mg) was mixed to 1000 mg paste to obtain a homogeneous dispersion for storage at 4°. The clusterin antisense oligonucleotide complexed with chitosan microparticles and incorporated into a **polymeric** paste loaded with **paclitaxel** induced tumor regression or inhibition of tumor growth in mice inoculated with LNCaP human prostate tumors for approx. 6 wk.

ST cationic **polymer** neg charged drug **controlled release**; chitosan oligonucleotide **controlled release** particle

IT **Medical goods**
(**catheters**; polycationic **polymers** for **controlled release** of neg. charged pharmacol. active compound)

IT Polyelectrolytes
(cationic; cationic **polymers** for **controlled release** of neg. charged pharmacol. active compound)

IT Drug delivery systems
(**controlled-release**; cationic **polymers** for **controlled release** of neg. charged pharmacol. active compound)

IT **Prosthetic materials and Prosthetics**
(**implants**; polycationic **polymers** for **controlled release** of neg. charged pharmacol. active compound)

IT Intestine, disease
(inflammatory, therapeutic agents for; polycationic **polymers** for **controlled release** of neg. charged pharmacol. active compound)

IT Bone
(metabolism of, agents for **control** of; polycationic **polymers** for **controlled release** of neg. charged pharmacol. active compound)

IT Drug delivery systems
(microparticles, **controlled-release**; cationic **polymers** for **controlled release** of neg. charged pharmacol. active compound)

IT Immunomodulators
(oligonucleotides; polycationic **polymers** for **controlled release** of neg. charged pharmacol. active compound)

IT Clusterin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(oligonucleotides; polycationic **polymers** for **controlled release** of neg. charged pharmacol. active compound)

IT Polyamines

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyamide-; polycationic **polymers** for **controlled release** of neg. charged pharmacol. active compound)

IT Polyamides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyamine-; polycationic **polymers** for **controlled release** of neg. charged pharmacol. active compound)

IT Anesthetics
Anti-inflammatory agents
Antiarthritics
Antiasthmatics
Antidiabetic agents
Antihistamines
Antihypertensives
Antihypotensives
Antimicrobial agents
Antitumor agents
Antitussives
Antiviral agents
Cardiotonics
Cardiovascular agents
Cat (Felis catus)
Cattle
Contact lenses
Dog (Canis familiaris)
Fungicides
Horse (Equus caballus)
Human
Hypnotics and Sedatives
Medical goods
Nervous system agents
Permeation enhancers
Prostate gland, neoplasm
Sheep
Vaccines
Vasoconstrictors
Vasodilators
(polycationic **polymers** for **controlled release** of neg. charged pharmacol. active compound)

IT Antisense oligonucleotides
Nucleic acids
Oligonucleotides
Phosphorothioate oligonucleotides
Ribozymes
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polycationic **polymers** for **controlled release** of neg. charged pharmacol. active compound)

IT Carbohydrates, biological studies
Enzymes, biological studies
Hormones, animal, biological studies
Ionene **polymers**
Protamines
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polycationic **polymers** for **controlled release** of neg. charged pharmacol. active compound)

IT Imines
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyimines; polycationic **polymers** for **controlled release** of neg. charged pharmacol. active compound)

IT **Artery, disease**
(**restenosis**, therapeutic agents for; polycationic **polymers** for **controlled release** of neg.

charged pharmacol. active compound)
IT Adhesion, biological
Eye, disease
Hepatitis
Multiple sclerosis
Psoriasis
(therapeutic agents for; polycationic **polymers** for **controlled release** of neg. charged pharmacol. active compound)
IT 59-05-2, Methotrexate 15663-27-1, Cisplatin **33069-62-4**, **Paclitaxel** 65271-80-9, Mitoxantrone 114977-28-5, Docetaxel
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polycationic **polymers** for **controlled release** of neg. charged pharmacol. active compound)
IT 79-10-7D, Acrylic acid, esters, **polymers** 79-41-4D, Methacrylic acid, esters, **polymers** 9003-39-8, Polyvinylpyrrolidone 9004-74-4, Methoxypolyethylene glycol 9005-25-8D, Starch, derivs. 9012-76-4, Chitosan 25086-42-4, Poly(p-aminostyrene) 25104-18-1, Polylysine 26062-48-6, Polyhistidine 26854-81-9, Polyhistidine 38000-06-5, Polylysine 72468-00-9
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polycationic **polymers** for **controlled release** of neg. charged pharmacol. active compound)
IT 188626-10-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(triblock; polycationic **polymers** for **controlled release** of neg. charged pharmacol. active compound)
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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(2) Cui, Z; JOURNAL OF CONTROLLED RELEASE 2001, V75(3), P409 HCAPLUS
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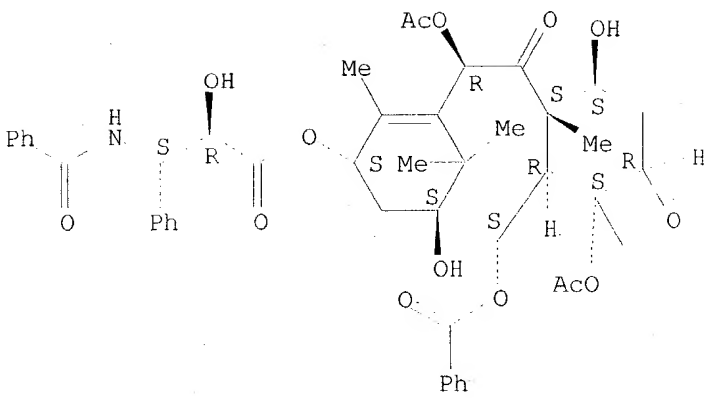
IT **33069-62-4, Paclitaxel**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polycationic **polymers** for **controlled release** of neg. charged pharmacol. active compound)
RN 33069-62-4 HCAPLUS
CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L61 ANSWER 7 OF 30 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:202525 HCAPLUS
DN 138:243276
ED Entered STN: 14 Mar 2003
TI Vascular implants containing combretastatin A-4 or combretastatin A-4 phosphate
IN Wnendt, Stephan; Chaplin, David; Kuttler, Bernd; Lorenz, Guenter
PA Oxygene Inc., USA
SO PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DT Patent
LA German
IC ICM A61L033-16
ICS A61L029-16; A61L027-54
CC 63-6 (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003020331	A1	20030313	WO 2002-EP9836	20020903
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	DE 10142897	A1	20030320	DE 2001-10142897	20010903
	DE 10142881	A1	20030403	DE 2001-10142881	20010903
PRAI	DE 2001-10142881	A	20010903		
	DE 2001-10142897	A	20010903		

AB The invention relates to implants, in particular intracavernous or intravascular implants, preferably for the treatment or prophylaxis of coronary or peripheral vascular occlusion, strictures or stenosis, in particular for the prophylaxis of **restenosis**. The implants contain combretastatin A-4 or combretastatin A-4 phosphate that is chemical bonded in a covalent or non-covalent form or is in a phys. fixed form. **Stents** prepared from alloys, **polymers** or their combination, also with alumina coating are treated with the alc. solution of combretastatin A-4 or combretastatin A-4 phosphate under sterile condition. According to an other method combretastatin A-4 or combretastatin A-4 phosphate are included in a **biodegradable polymer** for coating. Other drugs can be added to the implants.

ST vascular implant **stent** combretastatin A4
IT Platelet-derived growth factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Antagonists; vascular implants containing combretastatin A-4 or combretastatin A-4 phosphate)
IT Vascular endothelial growth factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(activators of; vascular implants containing combretastatin A-4 or combretastatin A-4 phosphate)
IT **Prosthetic materials and Prosthetics**
(alloys, **implants; vascular implants** containing combretastatin A-4 or combretastatin A-4 phosphate)
IT Angiotensin receptor antagonists
(angiotensin II; vascular implants containing combretastatin A-4 or combretastatin A-4 phosphate)
IT **Prosthetic materials and Prosthetics**
(cardiovascular **implants; vascular implants** containing combretastatin A-4 or combretastatin A-4 phosphate)
IT **Medical goods**
(**catheters**; vascular implants containing combretastatin A-4 or combretastatin A-4 phosphate)
IT **Prosthetic materials and Prosthetics**
(ceramics, ceramics coating; **vascular implants** containing combretastatin A-4 or combretastatin A-4 phosphate)
IT **Prosthetic materials and Prosthetics**
(composites, **implants; vascular implants** containing combretastatin A-4 or combretastatin A-4 phosphate)
IT **Artery, disease**
(**coronary, restenosis**; vascular implants containing combretastatin A-4 or combretastatin A-4 phosphate)
IT **Artery, disease**
(coronary, **stenosis**; vascular implants containing combretastatin A-4 or combretastatin A-4 phosphate)
IT **Prosthetic materials and Prosthetics**
(**implants**, intravascular; **vascular implants** containing combretastatin A-4 or combretastatin A-4 phosphate)
IT **Drug delivery systems**
(**implants**; vascular **implants** containing combretastatin A-4 or combretastatin A-4 phosphate)
IT **Prosthetic materials and Prosthetics**
(**polymers**; **vascular implants** containing combretastatin A-4 or combretastatin A-4 phosphate)
IT **Artery, disease**
(**restenosis**; vascular implants containing combretastatin A-4 or combretastatin A-4 phosphate)
IT **Artery, disease**
(**stenosis**; vascular implants containing combretastatin A-4 or combretastatin A-4 phosphate)
IT **Medical goods**
(**stents**; vascular implants containing combretastatin A-4 or combretastatin A-4 phosphate)
IT **Drug delivery systems**
(**sustained-release**; vascular **implants** containing combretastatin A-4 or combretastatin A-4 phosphate)
IT Human
(vascular implants containing combretastatin A-4 or combretastatin A-4 phosphate)
IT **Fluoropolymers**, biological studies
Polyester fibers, biological studies
Polyurethanes, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vascular implants containing combretastatin A-4 or combretastatin A-4

phosphate)
IT Corticosteroids, biological studies
Interleukin 10
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vascular implants containing combretastatin A-4 or combretastatin A-4 phosphate)
IT 329967-85-3, Cyclooxygenase 1
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(COX-1, inhibitors; vascular implants containing combretastatin A-4 or combretastatin A-4 phosphate)
IT 329900-75-6, COX-2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; vascular implants containing combretastatin A-4 or combretastatin A-4 phosphate)
IT 1344-28-1, Alumina, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coating for implants; vascular implants containing combretastatin A-4 or combretastatin A-4 phosphate)
IT 10102-43-9, Nitric oxide, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(donors; vascular implants containing combretastatin A-4 or combretastatin A-4 phosphate)
IT 9002-04-4, Thrombin 9015-82-1, Angiotensin-converting enzyme
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; vascular implants containing combretastatin A-4 or combretastatin A-4 phosphate)
IT 9054-75-5, Guanylate-Cyclase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(soluble, stimulants of; vascular implants containing combretastatin A-4 or combretastatin A-4 phosphate)
IT 9002-84-0, PTFE 25087-26-7, Methacrylic acid **homopolymer**
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vascular implants containing combretastatin A-4 or combretastatin A-4 phosphate)
IT 50-02-2, Dexamethasone 50-28-2, 17β-Estradiol, biological studies
50-76-0, Actinomycin D 52-53-9, Verapamil 53-03-2, Prednisone
53-86-1, Indomethacin 55-63-0, Nitroglycerin 59-05-2, Methotrexate
64-17-5, Ethanol, biological studies 67-56-1, Methanol, biological studies 86-54-4, Hydralazin 378-44-9, Betamethasone 865-21-4, Vinblastin 8001-27-2, Hirudin 14402-89-2, Sodium nitroprusside
15307-86-5, Diclofenac 15663-27-1, Cisplatin 15687-27-1, Ibuprofen
21829-25-4, Nifedipine 22204-53-1, Naproxen 23288-49-5, Probucol
24280-93-1, Mycophenolic acid 25717-80-0, Molsidomine **33069-62-4**
, **Paclitaxel** 33876-97-0, Linsidomine 42399-41-7, Diltiazem
53123-88-9, Rapamycin 53902-12-8, Tranilast 62571-86-2, Captopril
65271-80-9, Mitoxantrone 66085-59-4, Nimodipine 71125-38-7, Meloxicam
71142-71-7, PPACK 75847-73-3, Enalapril 76547-98-3, Lisinopril
79217-60-0, Cyclosporin 85441-61-8, Quinapril 104987-11-3, FK506
114798-26-4, Losartan 117048-59-6, Combretastatin A-4 123948-87-8, Topotecan 127464-60-2, Vascular endothelial growth factor 128270-60-0, Hirulog 137862-53-4, Valsartan 138402-11-6, Irbesartan 139481-59-7, Candesartan 140208-23-7, Plasminogen activator inhibitor I
143653-53-6, Rheopro 146426-40-6, Flavopiridol 159351-69-6, SDZ RAD
162011-90-7, Vioxx 169590-42-5, Celebrex 185681-64-5, 7-Hexanoyl-**Taxol** 222030-63-9, Combretastatin A-4 phosphate 256376-24-6, BAY 41-2272
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vascular implants containing combretastatin A-4 or combretastatin A-4 phosphate)
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE

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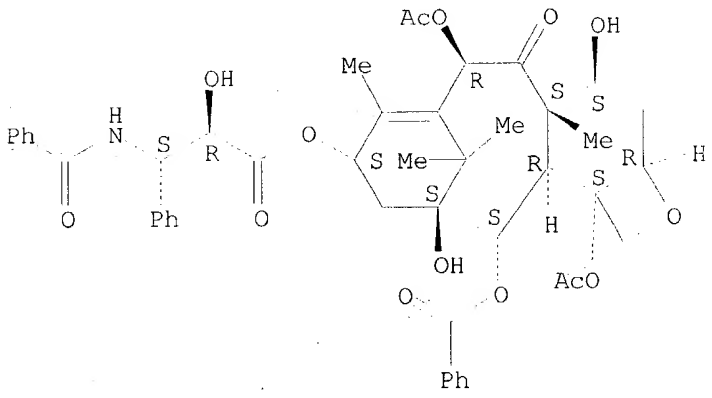
IT **33069-62-4, Paclitaxel**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vascular implants containing combretastatin A-4 or combretastatin A-4 phosphate)

RN 33069-62-4 HCAPLUS

CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L61 ANSWER 8 OF 30 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:132056 HCAPLUS
DN 139:219048
ED Entered STN: 21 Feb 2003
TI Inorganic materials as drug delivery systems in coronary artery stenting
AU Karoussos, I. A.; Wieneke, H.; Sawitowski, T.; Wnendt, S.; Fischer, A.; Dirsch, O.; Dahmen, U.; Erbel, R.
CS Department of Cardiology, University Essen, Germany
SO Materialwissenschaft und Werkstofftechnik (2002), 33(12), 738-746
CODEN: MATWER; ISSN: 0933-5137
PB Wiley-VCH Verlag GmbH & Co. KGaA
DT Journal; General Review
LA English
CC 63-0 (Pharmaceuticals)
AB A review and discussion. Recent studies proved coronary **stent** implantation to be superior over conventional **angioplasty** in the treatment of coronary artery disease. However, **restenosis** remains one of the most crucial problems in interventional cardiol. Inflammatory infiltrates and foreign body reactions can be found in the tissue surrounding the struts in stenting. Thrombogenesis, proliferation of α-actin expressing cells (smooth muscle cells) and hyperplasia of the intima occur. In order to improve the **biocompatibility** of the **stents**, new **stent** designs and **stent** coatings have been developed. One advantage of **stent** coating is the combination of mech. stability of the **stent** with the **biocompatibility** of the coating. The coatings are divided into active and passive coatings. Passive coatings improve the **biocompatibility** of the **stent**, while active coatings may suppress neointima proliferation by **releasing** anti-inflammatory

or antiproliferative substances. Immunosuppressive drugs (tacrolimus, sirolimus) and cytostatic drugs (**paclitaxel**) have been tested in several studies and showed promising results. However, it could also be demonstrated that **polymer**-coated **stents** used as a matrix for drug **release** reduced the hyperplasia of the intima. However, after dissipation of the immunosuppressants or cytostatics, the presence of the **polymer** itself lead to a delayed inflammation and proliferation causing **restenosis**. Thus, efforts have been made to develop inorg. coatings that are suitable for drug loading. One promising approach is a new nanoporous alumina coating. Preliminary tests with this coating revealed favorable loading characteristics and **sustained** drug **release** in vivo. The present article provides an overview on different approaches for **stent** coatings.

ST review inorg drug delivery system coronary artery stenting

IT Coating materials
(alumina; inorg. materials as drug delivery systems in coronary artery stenting)

IT **Artery, disease**
(**coronary, restenosis**; inorg. materials as drug delivery systems in coronary artery stenting)

IT Drug delivery systems
(inorg. materials as drug delivery systems in coronary artery stenting)

IT **Medical goods**
(**stents**; inorg. materials as drug delivery systems in coronary artery stenting)

IT 1344-28-1, Alumina, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inorg. materials as drug delivery systems in coronary artery stenting)

RE.CNT 84 THERE ARE 84 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L61 ANSWER 9 OF 30 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:5702 HCAPLUS
DN 138:61340
ED Entered STN: 05 Jan 2003
TI Zero-order prolonged release coaxial implants containing **biodegradable polymers**
IN Gibson, John W.; Tipton, Arthur J.; Holl, Richard J.; Meador, Stacey
PA Southern Biosystems, Inc., USA
SO PCT Int. Appl., 36 pp.
CODEN: PIXXD2

DT Patent
LA English
IC ICM A61F002-02
CC 63-6 (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003000156	A1	20030103	WO 2002-US19475	20020620
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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	US 2003007992	A1	20030109	US 2002-177997	20020621
PRAI	US 2001-300404P	P	20010622		
	US 2001-325623P	P	20010927		

AB A coaxial implant has been developed using entirely **biodegradable** **polymeric** materials. A coaxial implant is a device having a core containing drug, surrounded by a semi-permeable membrane that **controls** the rate of **release** from the core. The device is formed by extrusion, using a pre-milling and extruding step to maximize uniformity of drug dispersion within the **polymeric** material. In one embodiment, the **polymer** is processed to yield a semi-crystalline **polymer**, rather than an amorphous **polymer**. The core containing the drug and the **polymer** membrane(s) can be the same or different **polymer**. The **polymer** can be the same or different composition (i.e., both polycaprolactone, or both poly(lactide-co-glycolide) of different monomer ratios, or polycaprolactone outside of a core of poly(lactide)), of the same or different mol. wts., and of the same or different chemical structure (i.e., crystalline, semi-crystalline or amorphous). The core acts as a reservoir of drug, which partitions from the core **polymer** to form a saturated solution of at least 10% drug at the **polymer** membrane. **Biodegradable** coaxial implants for delivery or narcotic analgesics such as fentanyl or sufentanil were prepared containing polycaprolactone.

ST **biodegradable** polyester coaxial implant zero order release

IT **Polymers**, biological studies
RL: DEV (Device component use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**biodegradable**; zero-order prolonged release coaxial implants containing **biodegradable polymers**)

IT **Drug delivery systems**
(**implants**, **controlled-release**; zero-order prolonged **release** coaxial **implants** containing **biodegradable polymers**)

IT Dissolution
(rate; zero-order prolonged release coaxial implants containing **biodegradable polymers**)

IT **Artery**, **disease**
(**restenosis**, prevention of; zero-order prolonged release coaxial implants containing **biodegradable polymers**)

IT Analgesics
Extrusion of plastics and rubbers
Opioid antagonists
(zero-order prolonged release coaxial implants containing **biodegradable polymers**)

IT Polyoxyalkylenes, biological studies
RL: DEV (Device component use); MOA (Modifier or additive use); THU

(Therapeutic use); BIOL (Biological study); USES (Uses)
(zero-order prolonged release coaxial implants containing **biodegradable polymers**)

IT Polyesters, biological studies
RL: DEV (Device component use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(zero-order prolonged release coaxial implants containing **biodegradable polymers**)

IT Peptides, biological studies
Proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(zero-order prolonged release coaxial implants containing **biodegradable polymers**)

IT 25322-68-3, Peg
RL: DEV (Device component use); MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(zero-order prolonged release coaxial implants containing **biodegradable polymers**)

IT 437-38-7, Fentanyl 16590-41-3, Naltrexone 24980-41-4, Polycaprolactone 25248-42-4, Polycaprolactone 56030-54-7, Sufentanil
RL: DEV (Device component use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(zero-order prolonged release coaxial implants containing **biodegradable polymers**)

IT 465-65-6, Naloxone 9005-49-6, Heparin, biological studies
33069-62-4, Taxol
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(zero-order prolonged release coaxial implants containing **biodegradable polymers**)

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

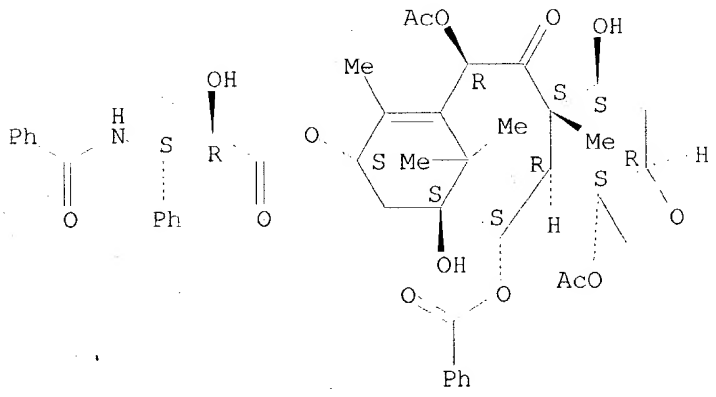
(1) Spicer; US 5340584 A 1994 HCAPLUS

IT **33069-62-4, Taxol**
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(zero-order prolonged release coaxial implants containing **biodegradable polymers**)

RN 33069-62-4 HCAPLUS

CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L61 ANSWER 10 OF 30 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:172 HCAPLUS
DN 139:207385
ED Entered STN: 01 Jan 2003
TI TAXUS I: Six - and twelve-month results from a randomized, double-blind trial on a slow-release **paclitaxel**-eluting **stent** for De Novo coronary lesions
AU Grube, Eberhard; Silber, Sigmund; Hauptmann, Karl Eugen; Mueller, Ralf; Buellesfeld, Lutz; Gerckens, Ulrich; Russell, Mary E.
CS Department of Cardiology and Angiology, Heart Center Siegburg, Siegburg, 53721, Germany
SO Circulation (2003), 107(1), 38-42
CODEN: CIRCAZ; ISSN: 0009-7322
PB Lippincott Williams & Wilkins
DT Journal
LA English
CC 1-8 (Pharmacology)
Section cross-reference(s): 63
AB The TAXUS NIRx **stent** (Boston Scientific Corp) provides local delivery of **paclitaxel** via a slow-**release** **polymer** coating. The TAXUS I trial was the first in-human experience evaluating safety and feasibility of the TAXUS NIRx **stent** system compared with bare NIR **stents** (**control**) (Boston Scientific Corp) for treatment of coronary lesions. The TAXUS I trial was a prospective, double-blind, three-center study randomizing 61 patients with de novo or restenotic lesions (≤12 mm) to receive a TAXUS (n = 31) vs. **control** (n = 30) **stent** (diameter 3.0 or 3.5 mm). Demographics, lesion characteristics, clin. outcomes were comparable between the groups. The 30-day major adverse cardiac event (MACE) rate was 0% in both groups (P = NS). No **stent** thromboses were reported at 1, 6, 9, or 12 mo. At 12 mo, the MACE rate was 3% (1 event) in the TAXUS group and 10% (4 events in 3 patients) in the **control** group (P = NS). Six-month angiog. **restenosis** rates were 0% for TAXUS vs. 10% for **control** (P = NS) patients. There were significant improvements in minimal lumen diameter (2.60 ± 0.49 vs. 2.19 ± 0.65 mm), diameter stenosis (13.56 ± 11.77 vs. 27.23 ± 16.69), and late lumen loss (0.36 ± 0.48 vs. 0.71 ± 0.48 mm) in the TAXUS group (all P ≤ 0.01). No evidence of edge **restenosis** was seen in either group. Intravascular ultrasound anal. showed significant improvements in normalized neointimal hyperplasia in the TAXUS (14.8 mm3) group compared with the **control** group (21.6 mm3) (P < 0.05). In this feasibility trial, the TAXUS slow-**release** **stent** was well tolerated and showed promise for treatment of coronary lesions, with significant redns. in angiog. and intravascular ultrasound measures of **restenosis**.
ST **stent** **paclitaxel** slow release clin trial
IT Cytotoxic agents
Human
(clin. trial of TAXUS I during six- and twelve-month results from a randomized, double-blind trial on a slow-release **paclitaxel**-eluting **stent** for De Novo coronary lesions)
IT **Artery, disease**
(**coronary, restenosis**; clin. trial of TAXUS I during six- and twelve-month results from a randomized, double-blind trial on a slow-release **paclitaxel**-eluting **stent** for De Novo coronary lesions)
IT Blood vessel, disease
(lesion, coronary; clin. trial of TAXUS I during six- and twelve-month results from a randomized, double-blind trial on a slow-release **paclitaxel**-eluting **stent** for De Novo coronary lesions)

IT Drug delivery systems
(slow-release; clin. trial of TAXUS I during six- and twelve-month results from a randomized, double-blind trial on a slow-release **paclitaxel**-eluting **stent** for De Novo coronary lesions)
IT **Medical goods**
(**stents**, TAXUS NIRx; clin. trial of TAXUS I during six- and twelve-month results from a randomized, double-blind trial on a slow-release **paclitaxel**-eluting **stent** for De Novo coronary lesions)
IT **33069-62-4, Paclitaxel**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(clin. trial of TAXUS I during six- and twelve-month results from a randomized, double-blind trial on a slow-release **paclitaxel**-eluting **stent** for De Novo coronary lesions)
RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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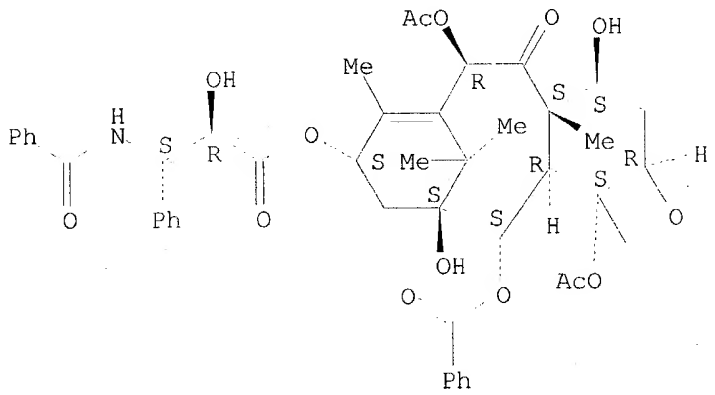
(11) Morice, M; N Engl J Med 2002, V346, P1773 HCAPLUS
(12) Sousa, J; Circulation 2001, V103, P192 HCAPLUS
IT **33069-62-4, Paclitaxel**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(clin. trial of TAXUS I during six- and twelve-month results from a randomized, double-blind trial on a slow-release **paclitaxel**-eluting **stent** for De Novo coronary lesions)
RN 33069-62-4 HCAPLUS
CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L61 ANSWER 11 OF 30 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:684247 HCAPLUS
DN 138:326407
ED Entered STN: 10 Sep 2002
TI Drug eluting **stents**: initial experiences
AU Grube, E.; Gerckens, U.; Muller, R.; Bullesfeld, L.
CS Heart-Center Siegburg, Siegburg, 53721, Germany
SO Zeitschrift fuer Kardiologie (2002), 91(Suppl. 3), 44-48
CODEN: ZKRDAX; ISSN: 0300-5860
PB Steinkopff Verlag
DT Journal
LA English
CC 63-5 (Pharmaceuticals)
AB Local delivery of immunosuppressive or antiproliferative agents using a drug-eluting **stent** is a new technol. meant to inhibit in-**stent restenosis** providing both a biol. and mech. solution and has recently emerged as a very promising approach. Up to now several agents have been in use: **Paclitaxel**, Rapamycin, Actinomycin D or Tacrolimus. Evaluating these drugs regarding their **release** kinetics, effective dosage, safety in clin. practice and benefit, several studies have been published or are still ongoing: SCORE (**Paclitaxel**-derivative), TAXUS I, II, III, IV (**Paclitaxel**), ELUTE, ASPECT (**Paclitaxel**), RAVEL, SIRIUS (Sirolimus), **ACTION** (Actinomycin), EVIDENT, PRESENT (Tacrolimus). **Paclitaxel** was the first **stent**-based antiproliferative agent under clin. investigation providing profound inhibition of neointimal thickening, depending on delivery duration and drug dosage. The randomized multicenter SCORE trail (Quanam **stent**, **Paclitaxel** coated) enrolled 266 patients at 17 sites. At 6 mo follow-up, a drop of 83% in **stent restenosis** using the drug-eluting **stent** could be achieved (6.4% drug-eluting **stent** vs. 36.9% **control** group) attributable to a remarkable decrease in intimal proliferation. Unfortunately, due to both frequent **stent** thrombosis and side-branch occlusions the reported 30-day MACE rate was 10.2%. The randomized TAXUS I safety trail (NIRx, **Paclitaxel** coated) also demonstrated beneficial reduction of restenotic lesions at 6-mo FU (0% vs. 11%) but, this time, associated with the absence of thrombotic events presumably due to the lower drug dosage. The ongoing TAXUS II, III and IV trails are aimed at providing addnl. insight regarding the efficacy of the TAXUS **Paclitaxel**-eluting **stent**. Both the RAVEL and the SIRIUS trial have been conducted to evaluate a Sirolimus-coated **stent** (Bx VELOCITY **stent**). From the results available, the beneficial findings regarding reduction of renarrowing using a drug-eluting **stent** have been confirmed without any adverse effects. Although parameters like drug toxicity, optimal drug dosage or delayed endothelial healing need to be further evaluated, summarizing the today's clin. experience the strategy of drug-coated **stents** promises a striking benefit in interventional treatment of coronary lesions.
ST **stent** antiproliferative **Paclitaxel** cardiovascular
IT Cardiovascular agents
Cytotoxic agents
Drug delivery systems
Human
(drug eluting **stents**)
IT **Medical goods**
(**stents**; drug eluting **stents**)
IT **33069-62-4, Paclitaxel**
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug eluting **stents**)
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
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(1) Albiero, R; Cardiology international 2000, V1, P39

(2) Axel, D; Circulation 1997, V96, P636 HCAPLUS
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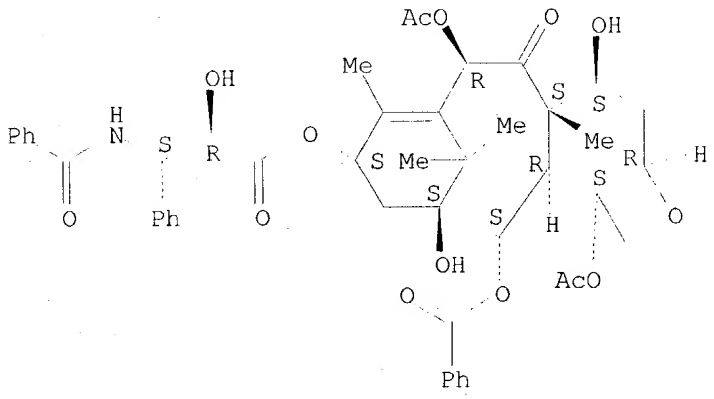
(9) Teirstein, P; N Engl J Med 1997, V336, P1697 MEDLINE
(10) Waksman, R; Circulation 1997, V96, P1944 MEDLINE

IT **33069-62-4, Paclitaxel**
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug eluting **stents**)

RN 33069-62-4 HCAPLUS

CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L61 ANSWER 12 OF 30 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:641861 HCAPLUS

DN 138:292487

ED Entered STN: 26 Aug 2002

TI Perspectives of drug-eluting **stents**. The next revolution

AU Moses, Jeffrey W.; Kipshidze, Nicholas; Leon, Martin B.

CS Lenox Hill Heart and Vascular Institute of New York and Cardiovascular Research Foundation, New York, NY, USA

SO American Journal of Cardiovascular Drugs (2002), 2(3), 163-172
CODEN: AJCDDJ; ISSN: 1175-3277

PB Adis International Ltd.

DT Journal; General Review

LA English

CC 63-0 (Pharmaceuticals)

AB A review. Coronary **stent** implantation has become a well established therapy in the management of coronary artery disease (CAD). Although the **Stent Restenosis** Study (STRESS) and Belgium-Netherlands **Stent** (BENESTENT) trials demonstrated convincingly that stenting is superior to percutaneous transluminal coronary **angioplasty** with respect to **restenosis** in de novo lesions, there is, however, still a high incidence (10 to 50%) of **restenosis** following **stent** implantation. Improvements in **stent** design and implantation techniques resulted in an increase in the use of coronary **stents** and today, in most

centers in the US and Europe, stenting has become the predominant form of nonsurgical revascularization accounting for about 80% of all percutaneous coronary intervention procedures. Coronary **stents** provide luminal scaffolding that virtually eliminates elastic recoil and remodeling. **Stents**, however, do not decrease neointimal hyperplasia and in fact lead to an increase in the proliferative comportment of **restenosis**. Agents that inhibit **cell** -cycle progression indirectly have also been tested as inhibitors of **vascular** proliferation. When coated onto **stents**, sirolimus, a macrolide antibiotic with immunosuppressive properties, and **paclitaxel** and dactinomycin, both chemotherapeutic agents, induced **cell**-cycle arrest in **smooth muscle** **cells** (SMC) and inhibited neointimal formation in animal models. Preliminary clin. studies with drug-eluting **stents** produced dramatic results eliminating **restenosis** in large and mid-size arteries. Quant. coronary angiog. and intravascular ultrasound demonstrated virtually complete inhibition of tissue growth at 6 and 12 mo after sirolimus-eluting **stent** implantation. Results are also very encouraging with **paclitaxel**-coated **stents**. However, it needs to be proven that current drug-eluting **stents** will produce similar results in 'real life' interventional practice (long lesions, lesions in small vessels, in vein grafts, chronic total occlusions, and bifurcated and ostial lesions). The ongoing randomized, double-blind sirolimus-coated Bx Velocity balloon expandable **stent** in the treatment of patients with de novo coronary artery lesions (SIRIUS) trial may answer some of these concerns. With further improvements, including the expansion of drug-loading capacity, double coatings and coatings with programmable pharmacokinetic capacity using advances in nanotechnol. (which may allow for more precise and **controlled** **release** of less toxic and improved mols.), we think that in the next few years the practice of interventional cardiol. may undergo major changes. A new era of dramatic improvements in the treatment of CAD may have dawned. The prospect of approval of this technol. should herald a host of clin. trials to revisit basic assumptions about the place of coronary stenting in the contemporary care of obstructive (and nonobstructive) CAD.

ST review **stent** cardiovascular drug delivery

IT Drug delivery systems
(**controlled-release**; perspectives of drug-eluting **stents**)

IT Cardiovascular agents
Drugs
Human
(perspectives of drug-eluting **stents**)

IT **Medical goods**
(**stents**; perspectives of drug-eluting **stents**)

RE.CNT 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L61 ANSWER 13 OF 30 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:487906 HCAPLUS
DN 137:68163
ED Entered STN: 28 Jun 2002
TI Delivery of therapeutic agents
IN Sirhan, Motasim; Yan, John
PA Avantec Vascular Corporation, USA
SO U.S. Pat. Appl. Publ., 49 pp.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61F002-06
ICS A61F002-00
NCL 623001150
CC 63-6 (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002082679	A1	20020627	US 2001-2595	20011101
	US 2002114823	A1	20020822	US 2001-782927	20010213
	US 6471980	B2	20021029		
	US 2003017190	A1	20030123	US 2002-242334	20020911
PRAI	US 2000-258024P	P	20001222		
	US 2001-782804	A	20010213		
	US 2001-782927	A	20010213		
	US 2001-783253	A	20010213		
	US 2001-783254	A	20010213		
	US 2001-308381P	P	20010726		

AB A device and a method using the device for reducing **restenosis** and hyperplasia after intravascular intervention are disclosed. The present invention also provides luminal prostheses which allow for **controlled release** of at least one therapeutic agent with increased efficacy to selected locations within a patient vasculature to reduce **restenosis**. An intraluminal prosthesis may comprise an expandable structure and a source adjacent the expandable structure for **releasing** the therapeutic capable agent into the body lumen to reduce smooth muscle cell proliferation. A therapeutic agent, mycophenolic acid, was prepared by dissolving it in acetone at 15 mg/mL. The amount of the drug agent varied in the range 0.1 μg-2 mg, preferably, at 600 μg. The drug solution was then coated onto or over a **stent** by spraying them with an atomizer sprayer, while the **stent** was rotated. The **stent** was allowed to let dry. The **stent** was then placed over the tri-fold balloon on a catheter and crimped thereon. After crimping, the drug remained intact and attached to the **stent**. Expansion of the **stent** against a simulated Tecoflex vessel showed no cracking of the drug.

ST therapeutic agent delivery implant; **polymer** therapeutic agent delivery implant

IT Platelet-derived growth factors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(B; delivery of therapeutic agents)

IT Imaging
(NMR; delivery of therapeutic agents)

IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aliphatic; delivery of therapeutic agents)

IT Growth factors, animal
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antagonists; delivery of therapeutic agents)

IT Blood vessel
(artificial; delivery of therapeutic agents)

IT Ion channel blockers
(calcium; delivery of therapeutic agents)

IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(caprolactone-based; delivery of therapeutic agents)
IT **Medical goods**
(**catheters**; delivery of therapeutic agents)
IT **Artery, disease**
(**coronary, restenosis**; delivery of therapeutic agents)
IT Angiogenesis
Angiogenesis inhibitors
Anti-inflammatory agents
Antibiotics
Anticoagulants
Antiemetics
Antimicrobial agents
Antioxidants
Antitumor agents
Antiviral agents
Artery
Blood vessel
Cytotoxic agents
Diffusion
Electric waves
Electromagnetic wave
Fibrosis
Gamma ray
Human
Hydrogels
Hydrolysis
Hyperplasia
Immunosuppressants
Inflammation
Magnetic field
Microwave
Platelet aggregation inhibitors
Psoriasis
Radical scavengers
Sound and Ultrasound
Spraying
Thrombolytics
Vasodilators
Wound healing promoters
X-ray
(delivery of therapeutic agents)
IT Metals, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(delivery of therapeutic agents)
IT Albumins, biological studies
Amino acids, biological studies
Antibodies
Collagens, biological studies
Fibrins
Fluoropolymers, biological studies
Gelatins, biological studies
Glucocorticoids
Glycolipids
Glycosaminoglycans, biological studies
Oligosaccharides, biological studies
Peptides, biological studies
Phospholipids, biological studies
Polyamides, biological studies
Polyamines

Polyanhydrides
Polyesters, biological studies
Polymers, biological studies
Polyoxyalkylenes, biological studies
Polyphosphazenes
Polysaccharides, biological studies
Polysiloxanes, biological studies
Polyurethanes, biological studies
Proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(delivery of therapeutic agents)

IT Blood vessel
(endothelium, cell; delivery of therapeutic agents)

IT **Drug delivery systems**
Prosthetic materials and Prosthetics
(**implants**; delivery of therapeutic agents)

IT Mitosis
(inhibitors; delivery of therapeutic agents)

IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lactic acid-based; delivery of therapeutic agents)

IT Anti-inflammatory agents
(nonsteroidal; delivery of therapeutic agents)

IT Drug delivery systems
(oral; delivery of therapeutic agents)

IT Polyethers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ortho ester group-containing; delivery of therapeutic agents)

IT Imines
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyimines; delivery of therapeutic agents)

IT Muscle
(smooth; delivery of therapeutic agents)

IT **Medical goods**
(**stents**; delivery of therapeutic agents)

IT Drug delivery systems
(transdermal; delivery of therapeutic agents)

IT Integrins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(αIIbβ3; delivery of therapeutic agents)

IT 7440-32-6, Titanium, biological studies 7440-47-3, Chromium, biological studies 7440-57-5, Gold, biological studies 12597-68-1, Stainless steel, biological studies 52013-44-2, Nitinol
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(delivery of therapeutic agents)

IT 50-02-2, Dexamethasone 50-18-0, Cyclophosphamide 50-35-1, Thalidomide 50-78-2, Acetylsalicylic acid 53-03-2, Prednisone 58-32-2, Dipyridamole 59-05-2, Methotrexate 83-43-2, Methylprednisolone 83-88-5, Riboflavin, biological studies 88-12-0, N-Vinyl-2-pyrrolidone, biological studies 107-73-3, Phosphorylcholine 108-31-6, Maleic anhydride, biological studies 127-07-1, Hydroxyurea 446-86-6, Azathioprine 1402-38-6, Actinomycin 1972-08-3, Dronabinol 7689-03-4, Camptothecin 9002-84-0 9002-86-2, Polyvinyl chloride 9002-98-6 9003-05-8, Polyacrylamide 9003-63-8, Poly(n-butyl methacrylate) 9004-34-6, Cellulose, biological studies 9004-36-8, Cellulose acetate butyrate 9005-49-6, Heparin, biological studies 9007-27-6, Chondroitin 9011-14-7, Poly(methyl methacrylate) 9016-00-6, Poly(dimethyl siloxane) 19545-26-7, Wortmannin 24280-93-1, Mycophenolic acid 24937-78-8, Ethylene-vinyl acetate **copolymer** 24980-41-4, Polycaprolactone 25067-34-9, Ethylene-vinyl alcohol **copolymer** 25189-52-0 25248-42-4, Polycaprolactone 25249-16-5, Poly(2-hydroxyethyl methacrylate) 25322-68-3, Polyethylene glycol 25722-33-2, Parylene

25736-86-1, Polyethylene glycol methacrylate 26009-03-0, Poly(glycolic acid) 26023-30-3, Poly(lactic acid) 26063-00-3, Poly(hydroxybutyrate) 26100-51-6, Poly(lactic acid) 26124-68-5, Poly(glycolic acid) 26744-04-7 29223-92-5 31621-87-1, Polydioxanone 31900-57-9, Poly(dimethyl siloxane) **33069-62-4, Taxol** 35284-36-7 38748-32-2, Triptolide 50924-49-7, Mizoribine 53123-88-9, Rapamycin 55142-85-3, Ticlopidine 59865-13-3, Cyclosporine 60084-10-8, Tiazofurin 66844-36-8, Caprolactone-L-lactic acid **copolymer** 67291-18-3, Poly(3-hydroxyvaleric acid), SRU 73963-72-1, Pletal 80137-67-3, Caprolactone-lactic acid **copolymer** 83120-66-5, Poly(3-hydroxyvaleric acid) 89149-10-0, Deoxyspergualin 95058-81-4, Gemcitabine 99614-02-5, Zofran 104987-11-3, Tacrolimus 104987-12-4, Ascomycin 105979-17-7, Benidipine 107007-99-8, Granisetron hydrochloride 113665-84-2, Clopidogrel 120202-66-6, Plavix 123948-87-8, Topotecan 128794-94-5, Mycophenolate mofetil 143653-53-6, Rheopro 152923-56-3, Daclizumab 154447-36-6, LY 294002 159351-69-6, Certican 162359-56-0, FTY 720 188627-80-7, Eptifibatide 439112-98-8, Parylast
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(delivery of therapeutic agents)

IT 10102-43-9, Nitrogen oxide (NO), biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(donors; delivery of therapeutic agents)

IT 58-64-0, ADP, biological studies 9036-21-9, Phosphodiesterase III 39391-18-9, Cyclooxygenase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; delivery of therapeutic agents)

IT 62229-50-9, Epidermal growth factor
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors; delivery of therapeutic agents)

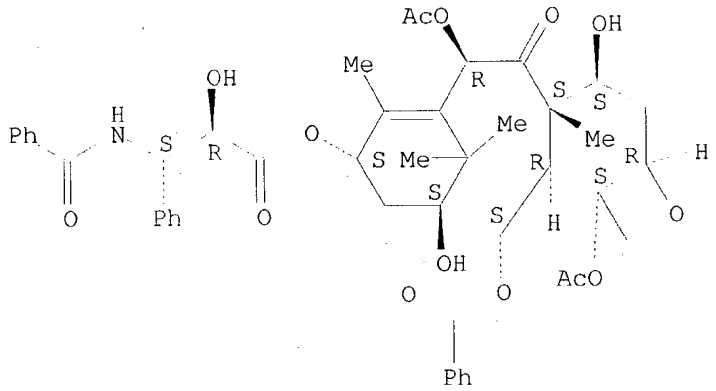
IT 58-61-7, Adenosine, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(reuptake inhibitors; delivery of therapeutic agents)

IT **33069-62-4, Taxol**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(delivery of therapeutic agents)

RN 33069-62-4 HCAPLUS

CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



AN 2002:465853 HCAPLUS
DN 137:37679
ED Entered STN: 21 Jun 2002
TI Drug delivery compositions and medical devices containing block **copolymer**
IN Pinchuk, Leonard; Nott, Sepideh; Schwarz, Marlene; Kamath, Kalpana
PA **SciMed Life Systems, Inc., USA**
SO PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61L
CC 63-6 (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002047731	A2	20020620	WO 2001-US48380	20011212
	WO 2002047731	A3	20030123		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2002107330	A1	20020808	US 2000-734639	20001212
	US 6545097	B2	20030408		
	AU 2002030851	A5	20020624	AU 2002-30851	20011212
	EP 1341565	A2	20030910	EP 2001-991102	20011212
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2003171496	A1	20030911	US 2002-319802	20021213
PRAI	US 2000-734639	A	20001212		
	WO 2001-US48380	W	20011212		

AB A composition for delivery of a therapeutic agent is provided. The composition comprises: (a) a **biocompatible** block **copolymer** comprising one or more elastomeric blocks and one or more thermoplastic blocks and (b) a therapeutic agent, wherein the block **copolymer** is loaded with the therapeutic agent. The block **copolymer** is preferably of the formula X-(AB)n, where A is an elastomeric block, B is thermoplastic block, n is a pos. whole number and X is a seed mol. The elastomeric blocks are preferably polyolefin blocks, and the thermoplastic blocks are preferably selected from vinyl aromatic blocks and methacrylate blocks. According to another aspect of the invention, a medical device is provided, at least a portion of which is insertable or implantable into the body of a patient. The medical device comprises (a) the above **biocompatible** block **copolymer** and (b) a therapeutic agent, wherein the block **copolymer** is loaded with the therapeutic agent. According to another aspect of the present invention, a method of treatment is provided in which the above device is implanted or inserted into a patient, resulting in the release of therapeutic agent in the patient over an extended period. According to yet another aspect of the invention, a coated medical device is provided which comprises: (a) an intravascular or intervascular medical device and (b) a coating over at least a portion of the intravascular or intervascular a medical device, wherein the coating comprises the above **biocompatible** block **copolymer**.

ST block polyolefin drug delivery medical device

IT **Artery**
(**angioplasty**; drug delivery compns. and medical devices containing block **copolymer**)

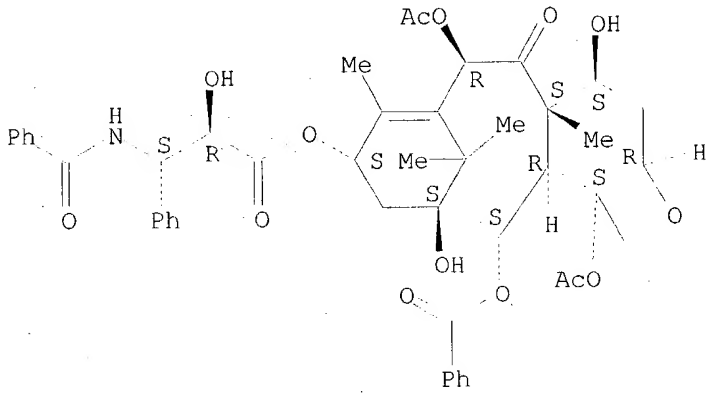
IT Blood vessel
(artificial; drug delivery compns. and medical devices containing block **copolymer**)
IT Polyolefins
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(block; drug delivery compns. and medical devices containing block **copolymer**)
IT **Medical goods**
(**catheters**; drug delivery compns. and medical devices containing block **copolymer**)
IT DNA
RNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(coding; drug delivery compns. and medical devices containing block **copolymer**)
IT Anesthetics
Anti-inflammatory agents
Anticholesteremic agents
Anticoagulants
Antitumor agents
Cytotoxic agents
Drug delivery systems
Extracellular matrix
Medical goods
Vasodilators
(drug delivery compns. and medical devices containing block **copolymer**)
IT Antisense DNA
Antisense RNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(drug delivery compns. and medical devices containing block **copolymer**)
IT Polyesters, biological studies
Polyolefin rubber
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug delivery compns. and medical devices containing block **copolymer**)
IT Synthetic rubber, biological studies
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(isobutylene-styrene; drug delivery compns. and medical devices containing block **copolymer**)
IT **Medical goods**
(**stents**; drug delivery compns. and medical devices containing block **copolymer**)
IT **33069-62-4, Paclitaxel**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug delivery compns. and medical devices containing block **copolymer**)
IT 24937-78-8, Eva 80137-67-3, Caprolactone-lactic acid **copolymer**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug delivery compns. and medical devices containing block **copolymer**)
IT 109671-82-1P, Isobutylene-styrene block **copolymer**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(triblock; drug delivery compns. and medical devices containing block **copolymer**)
IT **33069-62-4, Paclitaxel**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES

(Uses)
(drug delivery compns. and medical devices containing block **copolymer**)

RN 33069-62-4 HCAPLUS

CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L61 ANSWER 15 OF 30 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:271060 HCAPLUS
DN 136:299777
ED Entered STN: 11 Apr 2002
TI **Polymer** coating of medical devices using air suspension
IN Schwarz, Marlene; Miller, Kathleen; Kamath, Kalpana
PA **Scimed Life Systems, Inc., USA**
SO U.S., 15 pp., Cont.-in-part of U.S. Ser. No. 293,994, abandoned.
CODEN: USXXAM
DT Patent
LA English
IC ICM B01J013-00
NCL 427002150
CC 63-7 (Pharmaceuticals)
Section cross-reference(s): 42
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6368658	B1	20020409	US 2000-551614	20000417
	WO 2000062830	A2	20001026	WO 2000-US10316	20000418
	WO 2000062830	A3	20001228		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1171245	A2	20020116	EP 2000-926059	20000418
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2003524465	T2	20030819	JP 2000-611966	20000418

	US 2001022988	A1	20010920	US 2001-804040	20010313
	US 6607598	B2	20030819		
	US 2002127327	A1	20020912	US 2002-84868	20020301
PRAI	US 1999-293994	B2	19990419		
	US 2000-551614	A	20000417		
	WO 2000-US10316	W	20000418		
	US 2001-804040	A2	20010313		

AB Methods and apparatuses for coating medical devices and the devices thereby produced are disclosed. In one embodiment, the invention includes a method comprising the steps of suspending the medical device in an air stream and introducing a coating material into the air stream such that the coating material is dispersed therein and coats at least a portion of the medical device. In another embodiment, the medical devices are suspended in an air stream and a coating apparatus coats at least a portion of the medical device with a coating material. The coating apparatus may include a device that utilizes any number of alternative coating techniques for coating the medical devices. This process is used to apply one or more coating materials, simultaneously or in sequence. In certain embodiments of the invention, the coating materials include therapeutic agents, **polymers**, sugars, waxes, or fats. By using air suspensions to coat medical devices, the methods of the present invention result in coatings having minimal defects and uniform thicknesses and mech. properties. Further, the methods of the present invention are time efficient and cost effective because they facilitate the coating of numerous medical devices in a single batch, resulting in numerous medical device units containing substantially the same coating. For example, a coronary **stent** was coated in a fluidized bed chamber with a coating solution prepared by mixing 0.5-2.0% Elvax 40W, 0.05-0.6% **paclitaxel**, and balance chloroform. The **stents** had uniform coating layers in which **paclitaxel** was evenly distributed on each **stent** and substantially the same dose applied to every **stent** in the batch.

ST drug **polymer** air suspension coating medical good; **stent** air suspension coating drug **polymer**

IT Vapor deposition process
(UV-induced; **polymer** coating of medical devices using air suspension)

IT Coating process
(air suspension; **polymer** coating of medical devices using air suspension)

IT Quaternary ammonium compounds, biological studies
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(alkylbenzyldimethyl, chlorides; **polymer** coating of medical devices using air suspension)

IT Vapor deposition process
(chemical; **polymer** coating of medical devices using air suspension)

IT **Polymers**, biological studies
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(co-; **polymer** coating of medical devices using air suspension)

IT Ceramics
(coating device containing; **polymer** coating of medical devices using air suspension)

IT Metals, uses
RL: DEV (Device component use); USES (Uses)
(coating device containing; **polymer** coating of medical devices using air suspension)

IT DNA

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(compacting agents; **polymer** coating of medical devices using air suspension)

IT UV radiation
(deposition, **polymerization**, and treatment with; **polymer** coating of medical devices using air suspension)

IT **Polymerization**
(electron beam-induced; **polymer** coating of medical devices using air suspension)

IT Vapor deposition process
(electron-beam; **polymer** coating of medical devices using air suspension)

IT **Polymerization**
(graft, plasma; **polymer** coating of medical devices using air suspension)

IT Vapor deposition process
(ion plating; **polymer** coating of medical devices using air suspension)

IT Polyesters, biological studies
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(lactic acid-based; **polymer** coating of medical devices using air suspension)

IT **Polymerization**
Vapor deposition process
(microwave-induced; **polymer** coating of medical devices using air suspension)

IT Polyethers, biological studies
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(ortho ester group-containing; **polymer** coating of medical devices using air suspension)

IT Vapor deposition process
(photochem.; **polymer** coating of medical devices using air suspension)

IT Vapor deposition process
(plasma; **polymer** coating of medical devices using air suspension)

IT Coating apparatus
Crosslinking
Fluidized beds
Genetic vectors
Medical goods
(**polymer** coating of medical devices using air suspension)

IT Acrylic **polymers**, biological studies
Albumins, biological studies
Carbohydrates, biological studies
Fats and Glyceridic oils, biological studies
Gelatins, biological studies
Glycosaminoglycans, biological studies
Oligonucleotides
Peptides, biological studies
Polyamides, biological studies
Polyanhydrides
Polycarbonates, biological studies
Polyesters, biological studies
Polyethers, biological studies
Polymers, biological studies
Polyoxyalkylenes, biological studies
Polysaccharides, biological studies
Polysiloxanes, biological studies

Polyurethanes, biological studies
Proteins
Waxes
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**polymer** coating of medical devices using air suspension)

IT Vinyl compounds, biological studies
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**polymers**; **polymer** coating of medical devices using air suspension)

IT Nucleic acids
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(recombinant; **polymer** coating of medical devices using air suspension)

IT **Medical goods**
(**stents**, coronary; **polymer** coating of medical devices using air suspension)

IT Vapor deposition process
(thermal evaporation; **polymer** coating of medical devices using air suspension)

IT **Polymerization**
(thermal; **polymer** coating of medical devices using air suspension)

IT 111-30-8, Glutaraldehyde
RL: RCT (Reactant); RACT (Reactant or reagent)
(crosslinking agent; **polymer** coating of medical devices using air suspension)

IT 79-10-7D, Acrylic acid, esters, **polymers** 9002-88-4, Polyethylene 9002-89-5, Polyvinyl alcohol 9003-05-8, Polyacrylamide 9003-07-0, Polypropylene 9003-39-8, Polyvinylpyrrolidone 9003-53-6, Polystyrene 9004-34-6, Cellulose, biological studies 9004-65-3, Hydroxypropyl methyl cellulose 15663-27-1, Cisplatin 24937-72-2, Poly(maleic anhydride) 24937-78-8, Elvax 40W 24980-41-4, Polycaprolactone 25248-42-4, Polycaprolactone 25316-40-9, Doxorubicin hydrochloride 25322-68-3, Polyethylene oxide 26009-03-0, Poly(glycolic acid) 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26100-51-6, Poly(lactic acid) 26124-68-5, Poly(glycolic acid) 30280-72-9, Acrylic acid-methylene-bis-acrylamide **copolymer 33069-62-4**, **Paclitaxel** 35054-79-6D, **polymeric** derivs. 50853-48-0D, **polymeric** derivs. 51110-01-1, Somatostatin 303176-49-0, Corethane 50D
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**polymer** coating of medical devices using air suspension)

RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD

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(2) Anon; DE 3323418 1985
(3) Anon; WO 9617692 1996
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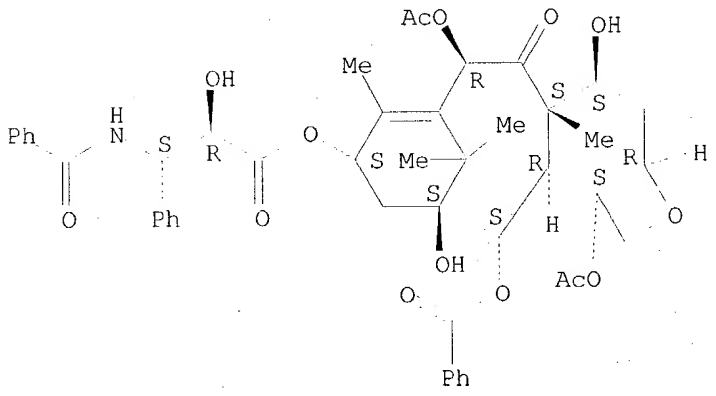
IT **33069-62-4, Paclitaxel**
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**polymer** coating of medical devices using air suspension)

RN 33069-62-4 HCAPLUS

CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L61 ANSWER 16 OF 30 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:108742 HCAPLUS
DN 136:374619
ED Entered STN: 10 Feb 2002

TI **Stent** development and local drug delivery
AU Regar, E.; Sianos, G.; Serruys, P. W.
CS Department of Cardiology, Thoraxcentre, Erasmus Medical Centre Rotterdam, Rotterdam, 3015 GD, Neth.
SO British Medical Bulletin (2001), 59, 227-248
CODEN: BMBUAQ; ISSN: 0007-1420
PB Oxford University Press
DT Journal; General Review
LA English
CC 63-0 (Pharmaceuticals)
Section cross-reference(s): 1
AB A review. **Stent** implantation has become the new standard **angioplasty** procedure. Instent re-stenosis remains the major limitation of coronary stenting. Re-stenosis is related to patient-, lesion- and procedure-specific factors. Patient-specific factors can not be influenced to any extent. Procedure-specific factors are affected by implantation technique and **stent** characteristics. Design and material influence **vascular** injury and humoral and cellular response. Radiation has been shown to have inhibitory effects on **smooth muscle cell** growth and neo-intima formation, but in clin. trials the outcome has been hampered by re-stenosis at the edges of the radioactive **stent** ("candy wrapper"). New approaches target pharmacol. modulation of local **vascular** biol. by local administration of drugs. This allows for drug application at the precise site and time of vessel injury. Systemic release is minimal and this may reduce the risk of toxicity. The drug and the delivery vehicle must fulfil pharmacol., pharmacokinetic and mech. requirements and the application of eluting degradable matrixes seems to be a possible solution Numerous pharmacol. agents with antiproliferative properties are currently under clin. investigation, e.g. actinomycin D, rapamycin or **paclitaxel**. Another approach is for **stents** to be made of **biodegradable** materials as an alternative to metallic **stents**. Their potential long-term complications, such as in-**stent restenosis** and the inaccessibility of the lesion site for surgical revascularization, needs to be assessed. Current investigational devices and the line of (pre)clin. investigation are discussed in detail. Currently, there is little exptl., and only preliminary clin., understanding of the acute and long-term effects of drug-eluting or **biodegradable stents** in coronary arteries. The clin. benefit of these approaches still has to be proven.
ST review **stent** development prosthetic implant drug targeting local delivery
IT **Artery, disease**
(**coronary, restenosis; stent** development and local drug delivery)
IT **Drug delivery systems**
(**implants, controlled-release; stent** development and local drug delivery)
IT Drug delivery systems
(local; **stent** development and local drug delivery)
IT Drug delivery systems
Drugs
Human
(**stent** development and local drug delivery)
IT **Medical goods**
(**stents; stent** development and local drug delivery)
RE.CNT 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD
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L61 ANSWER 17 OF 30 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:850997 HCAPLUS
DN 135:376782
ED Entered STN: 23 Nov 2001
TI Drug combinations for prevention of **restenosis**
IN Kopia, Gregory A.; Llanos, Gerald H.; Falotico, Robert F.
PA Cordis Corporation, USA
SO PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61L031-16
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
FAN.CNT 11

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001087372	A1	20011122	WO 2001-US13780	20010425
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 2001062957	A5	20011126	AU 2001-62957	20010425
	EP 1289576	A1	20030312	EP 2001-937196	20010425
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2003533493	T2	20031111	JP 2001-583836	20010425
PRAI	US 2000-204417P	P	20000512		
	US 2000-575480P	P	20000519		
	US 2000-575480	A	20000519		
	WO 2001-US13780	W	20010425		

AB The current invention comprises an approach to solving the clin. problem of **restenosis**, which involves the administration of combinations of drugs to patients undergoing PTCA or **stent** implantation. In one embodiment of the invention, an antiproliferative agent such as rapamycin, vincristine or **taxol** is administered in combination with the antiinflammatory agent, dexamethasone, to patients systemically, either s.c. or i.v. In another embodiment of the invention, the antiproliferative and antiinflammatory agents are bound in a single formulation to the surface of a **stent** by means of incorporation within either a **biodegradable** or biostable **polymeric** coating. Alternatively, such drug combinations could be incorporated into a **stent** constructed with a grooved reservoir. **Stents** were coated with Parylene-C by using a vapor deposition method. The

stent was weighed and then mounted for coating. While the **stent** was rotating a solution of 1.75 mg/mL poly(ethylene-co-vinyl acetate) (PEVA), 1.75 mg/mL poly(Bu methacrylate), 0.75 mg/mL rapamycin and 0.75 mg/mL dexamethasone dissolved in THF was sprayed onto it. The coated **stent** was removed from the spray and allowed to air-dry. After a final weighing the amount of coating on the **stent** was determined

ST drug combination **restenosis** prevention; antiinflammatory combination **restenosis** prevention; rapamycin dexamethasone **polymer restenosis** prevention

IT **Medical goods**
(**catheters**; drug combinations for prevention of **restenosis**)

IT Drug delivery systems
(**controlled-release**; drug combinations for prevention of **restenosis**)

IT **Artery**
(coronary, **angioplasty**, inhibitors; drug combinations for prevention of **restenosis**)

IT **Artery, disease**
(**coronary**, **restenosis**; drug combinations for prevention of **restenosis**)

IT Anti-inflammatory agents
Drug delivery systems
(drug combinations for prevention of **restenosis**)

IT Cytokines
Growth factors, animal
Polymers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug combinations for prevention of **restenosis**)

IT Extracellular matrix
Signal transduction, biological
(inhibitors; drug combinations for prevention of **restenosis**)

IT Proliferation inhibition
(proliferation inhibitors; drug combinations for prevention of **restenosis**)

IT **Medical goods**
(**stents**; drug combinations for prevention of **restenosis**)

IT 50-02-2, Dexamethasone 57-22-7, Vincristine 9003-63-8, Poly(butyl methacrylate) 9052-19-1, Parylene C 24937-78-8, EVA **33069-62-4**, **Taxol** 53123-88-9, Rapamycin 55837-20-2, Halofuginone 192185-68-5, R 115777
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug combinations for prevention of **restenosis**)

IT 80449-02-1, Tyrosine kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; drug combinations for prevention of **restenosis**)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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(5) Scimed Life Systems Inc; WO 0027445 A 2000
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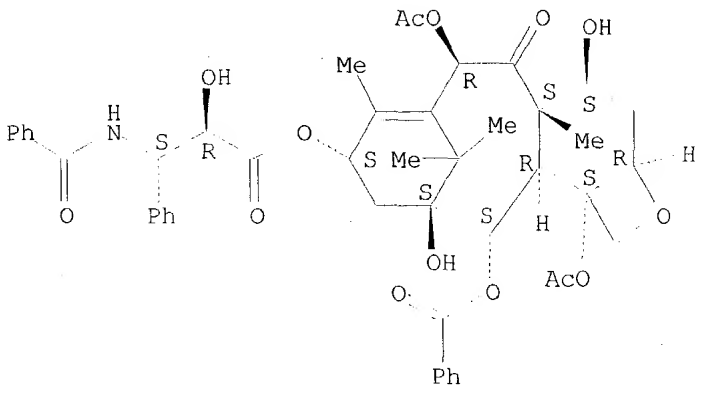
IT **33069-62-4, Taxol**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug combinations for prevention of **restenosis**)

RN 33069-62-4 HCAPLUS

CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-

tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L61 ANSWER 18 OF 30 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:830888 HCAPLUS
DN 135:362645
ED Entered STN: 15 Nov 2001
TI Bioresorbable hydrogel compositions for implantable prostheses
IN Loomis, Gary L.; Lentz, D. Christian
PA **Scimed Life Systems, Inc., USA**
SO U.S., 11 pp., Cont.-in-part of U.S. 6,028,164.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61L027-00
ICS A61L029-00; A61L031-00; A61F002-12; A61K006-00
NCL 523105000
CC 63-7 (Pharmaceuticals)
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6316522	B1	20011113	US 1999-395725	19990914
	US 5854382	A	19981229	US 1997-914130	19970818
	US 6005020	A	19991221	US 1998-145588	19980902
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	US 2002035168	A1	20020321	US 2001-957427	20010920
	US 6534560	B2	20030318		
	US 2003162861	A1	20030828	US 2003-369777	20030219
	US 6660827	B2	20031209		
PRAI	US 1997-914130	A3	19970818		
	US 1998-145588	A1	19980902		
	US 1999-243379	A2	19990201		
	US 1999-395725	A1	19990914		
	US 2001-957427	A1	20010920		

AB Crosslinked compns. formed from water-insol. **copolymers** are disclosed. These compns. are **copolymers** having a bioresorbable region, a hydrophilic region and at least two cross-linkable functional groups per **polymer** chain. Crosslinking of these **polymers** can be effected in solution in organic solvents or in solvent-free systems. If crosslinking occurs in a humid environment, a hydrogel will form. If crosslinking occurs in a non-humid environment, a xerogel will form which will form a hydrogel when exposed to a humid environment and the resulting crosslinked materials form hydrogels when exposed to humid environments. These hydrogels are useful as components

in medical devices such as implantable prostheses. In addition, such hydrogels are useful as delivery vehicles for therapeutic agents and as scaffolding for tissue engineering applications. The claimed water-insol. **copolymers** include lactide-oxirane **copolymer** dimethacrylate and lactide-methyloxirane-oxirane **copolymer** dimethacrylate.

ST bioresorbable hydrogel prosthetic implant; drug carrier bioresorbable hydrogel

IT Glycosides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino; bioresorbable hydrogels as drug carriers and as coating agents for medical goods and prosthetics)

IT Nutrients
(anti-; bioresorbable hydrogels as drug carriers and as coating agents for medical goods and prosthetics)

IT Artery
Blood vessel
(artificial; bioresorbable hydrogels as drug carriers and as coating agents for medical goods and prosthetics)

IT Alkylating agents, biological
Angiogenesis inhibitors
Anti-inflammatory agents
Antibiotics
Anticoagulants
Antitumor agents
Antiviral agents
Coating materials
Drug delivery systems
Hydrogels
(bioresorbable hydrogels as drug carriers and as coating agents for medical goods and prosthetics)

IT Alkaloids, biological studies
Angiogenic factors
Enzymes, biological studies
Hormones, animal, biological studies
Interferons
Sulfonamides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bioresorbable hydrogels as drug carriers and as coating agents for medical goods and prosthetics)

IT **Medical goods**
(**catheters**; bioresorbable hydrogels as drug carriers and as coating agents for medical goods and prosthetics)

IT Electric conductors
(for medical goods; bioresorbable hydrogels as drug carriers and as coating agents for medical goods and prosthetics)

IT **Prosthetic materials and Prosthetics**
(**implants**; bioresorbable hydrogels as drug carriers and as coating agents for medical goods and prosthetics)

IT Cell cycle
(regulators; bioresorbable hydrogels as drug carriers and as coating agents for medical goods and prosthetics)

IT **Medical goods**
(**stents**; bioresorbable hydrogels as drug carriers and as coating agents for medical goods and prosthetics)

IT Medical goods
(trocars; bioresorbable hydrogels as drug carriers and as coating agents for medical goods and prosthetics)

IT Medical goods
(wires; bioresorbable hydrogels as drug carriers and as coating agents for medical goods and prosthetics)

IT 372963-03-6P, Lactide-methyloxirane-oxirane block **copolymer** diacrylate

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(bioresorbable hydrogels as drug carriers and as coating agents for medical goods and prosthetics)

IT 50-18-0, Cyclophosphamide 50-44-2, 6-Mercaptopurine 51-21-8, 5-Fluorouracil 51-75-2, Mechlorethamine 54-42-2, Idoxuridine 56-75-7, Chloramphenicol 57-22-7, Vincristine 59-05-2, Methotrexate 60-54-8, Tetracycline 70-00-8, Trifluridine 114-07-8, Erythromycin 147-94-4, Cytarabine 148-82-3, Melphalan 154-21-2, Lincomycin 154-93-8, Carmustine 305-03-3, Chlorambucil 768-94-5, Amantadine 865-21-4, Vinblastine 1404-00-8, Mitomycin 1404-90-6, Vancomycin 1406-05-9, Penicillin 1406-11-7, **Polymyxin** 3778-73-2, Ifosfamide 4428-95-9, Foscarnet 5536-17-4, Vidarabine 8001-27-2, Hirudin 9002-01-1, Streptokinase 9005-49-6, Heparin, biological studies 9007-28-7, Chondroitin sulfate 9015-68-3, Asparaginase 9039-53-6, Urokinase 9050-30-0, Heparan sulfate 10540-29-1, Tamoxifen 11056-06-7, Bleomycin 11111-12-9, Cephalosporin 13010-20-3, Nitrosourea 13010-47-4, Lomustine 13311-84-7, Flutamide 13392-28-4, Rimantadine 15663-27-1, Cisplatin 18323-44-9, Clindamycin 20830-81-3, Daunomycin 23214-92-8, Doxorubicin 24967-94-0, Dermatan sulfate 30516-87-1, Zidovudine **33069-62-4**, **Paclitaxel** 33419-42-0, Etoposide 36791-04-5, Ribavirin 59277-89-3, Acyclovir 82410-32-0, Ganciclovir 114977-28-5, Docetaxel 169799-44-4, Keratin sulfate 364591-16-2, Lactide-poe block **copolymer** dimethacrylate 372963-02-5, Lactide-methyloxirane-oxirane block **copolymer** dimethacrylate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bioresorbable hydrogels as drug carriers and as coating agents for medical goods and prosthetics)

RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD

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(31) Rhodes; US 5843160 1998
(32) Spinu; US 5202413 1993 HCAPLUS

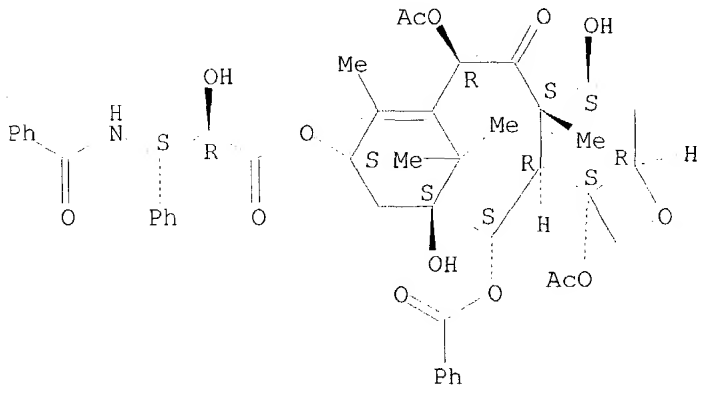
(33) Stone; US 5306311 1994

IT **33069-62-4, Paclitaxel**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bioresorbable hydrogels as drug carriers and as coating agents for medical goods and prosthetics)

RN 33069-62-4 HCAPLUS

CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L61 ANSWER 19 OF 30 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2001:564887 HCAPLUS

DN 135:142255

ED Entered STN: 03 Aug 2001

TI Drug delivery systems for treatment of **restenosis** and anastomotic intimal hyperplasia

IN Helmus, Michael N.; Cunanan, Crystal; Tremble, Patrice

PA Edwards Lifesciences Corporation, USA

SO PCT Int. Appl., 56 pp.
CODEN: PIXXD2

DT Patent

LA English

IC ICM A61L031-16
ICS A61L031-14; A61L031-04; A61L027-22; A61L027-54

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001054748	A1	20010802	WO 2001-US2563	20010125

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1250166	A1	20021023	EP 2001-905081	20010125

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2003520830 T2 20030708 JP 2001-554731 20010125
PRAI US 2000-178087P P 20000125
WO 2001-US2563 W 20010125

AB The invention provides methods for treating injuries to 1 or more internal structures of a subject by administering a drug delivery vehicle to an external surface of the injured structure. The drug delivery vehicle substantially adheres to the site of administration and provides for the **release** of a bioactive agent that reduces or prevents further injury to the internal structure by disease processes, such as hyperplasia. Thus, a fibrin **polymer** formulation, **polymd** . from a mixture containing a final concentration of 25-30 mg/mL fibrinogen, 5 IU human factor XIII, 50 IU human thrombin, and **paclitaxel** was prepared Also, each vial of **paclitaxel** formulated in delayed-**release** microspheres was reconstituted with 4 mL sterile saline, and 2 mL of this mixture was added per vial of a Sealant Protein Concentrate Anal. of the data obtained by angiog. suggested there was no significant difference between **control**, vehicle and **paclitaxel** treatment groups.

ST drug delivery **restenosis** anastomotic intimal hyperplasia; **polymer** drug delivery

IT Ion channel blockers
(calcium; drug delivery systems for treatment of **restenosis** and anastomotic intimal hyperplasia)

IT **Artery, disease**
(**coronary, restenosis**; drug delivery systems for treatment of **restenosis** and anastomotic intimal hyperplasia)

IT Anti-inflammatory agents
Anticoagulants
Antioxidants
Antitumor agents
Drug delivery systems
Immunosuppressants
Intestine
Platelet aggregation inhibitors
Sequestering agents
(drug delivery systems for treatment of **restenosis** and anastomotic intimal hyperplasia)

IT Albumins, biological studies
Antisense oligonucleotides
Corticosteroids, biological studies
Fibronectins
Gelatins, biological studies
Growth factors, animal
Polyamides, biological studies
Polyanhydrides
Polycarbonates, biological studies
Polyesters, biological studies
Polymers, biological studies
Polyoxyalkylenes, biological studies
Polyphosphazenes
Polysaccharides, biological studies
Polyurethanes, biological studies
Taxanes
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug delivery systems for treatment of **restenosis** and anastomotic intimal hyperplasia)

IT Drug delivery systems
(foams; drug delivery systems for treatment of **restenosis** and anastomotic intimal hyperplasia)

IT Collagens, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(formation, inhibitors; drug delivery systems for treatment of

restenosis and anastomotic intimal hyperplasia)
IT Drug delivery systems
(gels; drug delivery systems for treatment of **restenosis** and anastomotic intimal hyperplasia)
IT Drug delivery systems
(hydrogels; drug delivery systems for treatment of **restenosis** and anastomotic intimal hyperplasia)
IT **Prosthetic materials and Prosthetics**
(**implants**; drug delivery systems for treatment of **restenosis** and anastomotic intimal hyperplasia)
IT Fibrosis
Microtubule
(inhibitors; drug delivery systems for treatment of **restenosis** and anastomotic intimal hyperplasia)
IT Cytokines
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors; drug delivery systems for treatment of **restenosis** and anastomotic intimal hyperplasia)
IT **Artery, disease**
(intima, hyperplasia; drug delivery systems for treatment of **restenosis** and anastomotic intimal hyperplasia)
IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lactic acid-based; drug delivery systems for treatment of **restenosis** and anastomotic intimal hyperplasia)
IT Drug delivery systems
(microcapsules; drug delivery systems for treatment of **restenosis** and anastomotic intimal hyperplasia)
IT Polyethers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ortho ester group-containing; drug delivery systems for treatment of **restenosis** and anastomotic intimal hyperplasia)
IT Polyamides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(poly(amino acids); drug delivery systems for treatment of **restenosis** and anastomotic intimal hyperplasia)
IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyamide-; drug delivery systems for treatment of **restenosis** and anastomotic intimal hyperplasia)
IT Polyamides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyester-; drug delivery systems for treatment of **restenosis** and anastomotic intimal hyperplasia)
IT Polyurethanes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyurea-; drug delivery systems for treatment of **restenosis** and anastomotic intimal hyperplasia)
IT Polyureas
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyurethane-; drug delivery systems for treatment of **restenosis** and anastomotic intimal hyperplasia)
IT Fibrins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sealants; drug delivery systems for treatment of **restenosis** and anastomotic intimal hyperplasia)
IT Muscle
(smooth, inhibitors; drug delivery systems for treatment of **restenosis** and anastomotic intimal hyperplasia)
IT **Medical goods**
(**stents**; drug delivery systems for treatment of **restenosis** and anastomotic intimal hyperplasia)
IT Proteoglycans, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sulfated; drug delivery systems for treatment of **restenosis** and anastomotic intimal hyperplasia)

IT Drug delivery systems
(suspensions; drug delivery systems for treatment of **restenosis** and anastomotic intimal hyperplasia)

IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(thio-; drug delivery systems for treatment of **restenosis** and anastomotic intimal hyperplasia)

IT Heart
(valve; drug delivery systems for treatment of **restenosis** and anastomotic intimal hyperplasia)

IT Integrins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(αIIbβ3; drug delivery systems for treatment of **restenosis** and anastomotic intimal hyperplasia)

IT **33069-62-4, Paclitaxel**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug delivery systems for treatment of **restenosis** and anastomotic intimal hyperplasia)

IT 50-02-2, Dexamethasone 50-02-2D, Dexamethasone, derivs. 107-92-6D, Butyric acid, **polymers** 109-52-4D, Valeric acid, **polymers** 142-62-1D, Caproic acid, **polymers** 1605-68-1, Taxane 8001-27-2, Hirudin 8001-27-2D, Hirudin, derivs. 9002-04-4, Thrombin 9004-61-9, Hyaluronic acid 9004-65-3, HPMC 9005-49-6, Heparin, biological studies 9005-49-6D, Heparin, derivs., biological studies 10102-43-9, Nitrogen oxide (NO), biological studies 25322-68-3, Polyethylene glycol 26009-03-0, Poly(glycolic acid) 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26100-51-6, Poly(lactic acid) 26124-68-5, Poly(glycolic acid) 55837-20-2, Halofuginone 55837-20-2D, Halofuginone, derivs. 106392-12-5, Pluronic 194554-71-7, Tissue factor inhibitor
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug delivery systems for treatment of **restenosis** and anastomotic intimal hyperplasia)

IT 9054-89-1, superoxide dismutase
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mimics; drug delivery systems for treatment of **restenosis** and anastomotic intimal hyperplasia)

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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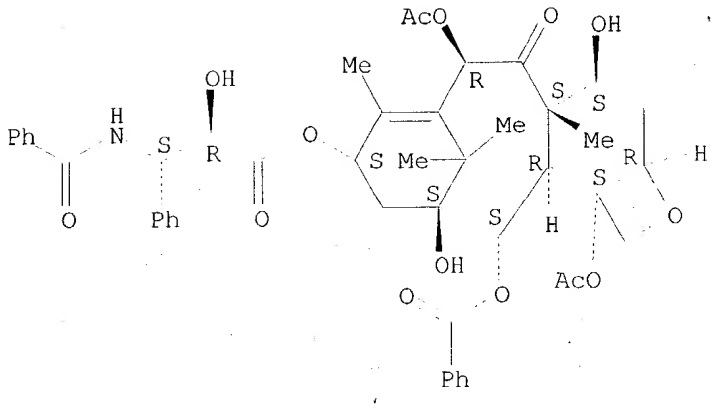
(2) Angiotech Pharm Inc; WO 9921908 A 1999 HCAPLUS
(3) Edwards, S; WO 9851369 A 1998
(4) Ethicon Inc; EP 0970711 A 2000 HCAPLUS
(5) Incept Llc; WO 0009088 A 2000 HCAPLUS

IT **33069-62-4, Paclitaxel**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug delivery systems for treatment of **restenosis** and anastomotic intimal hyperplasia)

RN 33069-62-4 HCAPLUS

CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L61 ANSWER 20 OF 30 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:507575 HCAPLUS
DN 135:97493
ED Entered STN: 13 Jul 2001
TI Controlled delivery of therapeutic agents by insertable medical devices
IN Li, Wei-Pin; Mao, Hai-Quan; Leong, Kam W.
PA USA
SO PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61L029-16
ICS A61L031-16
CC 63-6 (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001049338	A1	20010712	WO 2001-US25	20010102
	W: AU, CA, JP				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
	US 2002061326	A1	20020523	US 2001-750779	20010102
PRAI	US 1999-173743P	P	19991230		

AB A medical device and method for transportation and **release** of a therapeutic agent into a mammalian body are disclosed. The medical device is coated with alternating layers of a neg. charged therapeutic agent and a cationic polyelectrolyte, following a **controlled** adsorption technique. The method is simple, with minimal perturbation to the therapeutic agent and uses clin. acceptable **biopolymers** such as human serum albumin. The amount of the therapeutic agent that can be delivered by this technique is optimized by the number of the layers of the therapeutic agent adsorbed on the surface of medical device. There is a washing step between alternate layers of the therapeutic agent and cationic polyelectrolyte carrier, so that the amount of the therapeutic agent on the insertable medical device represents the portion that is stably entrapped and adsorbed on to the medical device. The insertable medical device and method according to this invention are capable of reproducibly delivering therapeutic agent to a site in a mammalian body, and allow for a highly reproducible and **controllable** **release** kinetics of the therapeutic agent. Multilayered films of DNA were built up on various neg. charged, neutral, and pos. charged surfaces, by spraying or dipping. The DNA adsorbed by human serum albumin or gelatin was **released** quickly while, due to the hydrophobicity of chitosan at neutral pH, the DNA adsorbed by chitosan was **released** very slowly.

ST medical device insert controlled delivery therapeutic agent
IT Ion channel blockers
(calcium; controlled delivery of therapeutic agents by insertable medical devices)
IT **Medical goods**
(**catheters**; controlled delivery of therapeutic agents by insertable medical devices)
IT Polyelectrolytes
(cationic; controlled delivery of therapeutic agents by insertable medical devices)
IT Anesthetics
Angiogenesis
Angiogenesis inhibitors
Anti-inflammatory agents
Anticholesteremic agents
Anticoagulants
Antimicrobial agents
Antitumor agents
Medical goods
Vasodilators
Virus vectors
(controlled delivery of therapeutic agents by insertable medical devices)
IT Bone morphogenetic proteins
DNA
Gelatins, biological studies
Nucleotides, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled delivery of therapeutic agents by insertable medical devices)
IT **Drug delivery systems**
(**implants, controlled-release**; **controlled** delivery of therapeutic agents by insertable medical devices)
IT Antioxidants
(pharmaceutical; controlled delivery of therapeutic agents by insertable medical devices)
IT **Artery, disease**
(**restenosis**, inhibitors; controlled delivery of therapeutic agents by insertable medical devices)
IT Albumins, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(serum; controlled delivery of therapeutic agents by insertable medical devices)
IT Proliferation inhibition
(smooth muscle; controlled delivery of therapeutic agents by insertable medical devices)
IT Muscle
(smooth, cell proliferation inhibitors; controlled delivery of therapeutic agents by insertable medical devices)
IT **Medical goods**
(**stents**; controlled delivery of therapeutic agents by insertable medical devices)
IT Human adenovirus
(vectors; controlled delivery of therapeutic agents by insertable medical devices)
IT 9012-76-4, Chitosan **33069-62-4, Paclitaxel**
RL: DEV (Device component use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled delivery of therapeutic agents by insertable medical devices)

IT 10102-43-9, Nitric oxide, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(donors; controlled delivery of therapeutic agents by insertable medical devices)
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Boston Scient Corp; WO 9908729 A 1999 HCAPLUS
(2) Dosio, F; JOURNAL OF CONTROLLED RELEASE 1997, V47(3), P293 HCAPLUS
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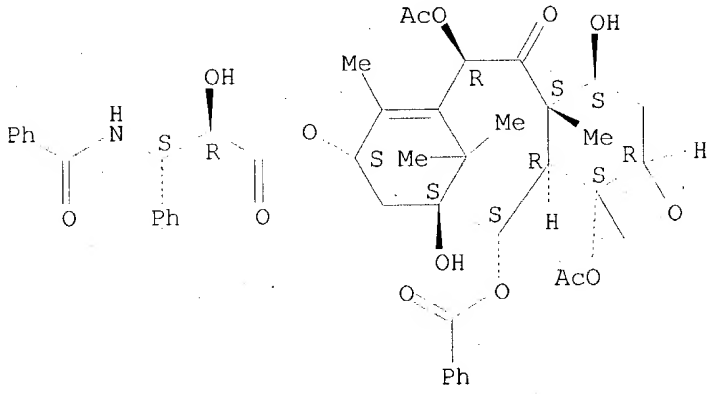
(4) Scimed Life Systems Inc; WO 9959649 A 1999 HCAPLUS
(5) Scimed Life Systems Inc; WO 0062830 A 2000 HCAPLUS
IT **33069-62-4, Paclitaxel**
RL: DEV (Device component use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled delivery of therapeutic agents by insertable medical devices)
RN 33069-62-4 HCAPLUS
CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L61 ANSWER 21 OF 30 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:352156 HCAPLUS
DN 134:357609
ED Entered STN: 17 May 2001
TI **Stents** with hybrid coating containing a **polymer**, a crosslinking agent, and a therapeutic agent for medical devices
IN Zhong, Sheng-ping
PA **Scimed Life Systems, Inc., USA**
SO U.S., 8 pp., Cont.-in-part of U.S. 6,048,620.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61I002-06
ICS A61L027-00; A61L033-00
NCL 623001420
CC 63-7 (Pharmaceuticals)
Section cross-reference(s): 1
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6231600	B1	20010515	US 1999-320340	19990526

US 5702754 A 19971230 US 1995-392141 19950222
US 6048620 A 20000411 US 1997-929948 19970915
PRAI US 1995-392141 A3 19950222
US 1997-929948 A2 19970915

AB A device such as a **stent** is provided with a hybrid coating including a time released, **restenosis** inhibiting coating and a non-thrombogenic coating to prevent clotting on the device. One first coat or layer includes a **polymer**, a crosslinking agent, and **paclitaxel**, analogs, or derivs. thereof. The first coat preferably includes a **polymer** having **Taxol** admixed therein so as to be releasable over time. The first coat preferably includes a polyfunctional aziridine as the crosslinking agent. The second coat preferably includes heparin to inhibit clot formation on the device. The crosslinking agent can covalently bond to both the first coat **polymer** and the second coat heparin. A **stent** can be provided with a first coat including an aqueous dispersion or emulsion of a **polymer** and an excess of crosslinking agent. The first coating can be dried, leaving a water insol. **polymer** coating. A second aqueous coating including a solution or dispersion of heparin can be applied over the first coating, the heparin becoming covalently bound to the crosslinking agent on the first coating surface. The resulting **stent** can inhibit **restenosis** while preventing blood clot formation on the **stent.**

ST **polymer** crosslinking agent drug **stent** coating; antithrombotic heparin **paclitaxel polymer** **stent** coating

IT Polyurethanes, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(acrylates; **stents** with hybrid coating containing **polymer**, crosslinking agent, and therapeutic agent)

IT **Prosthetic materials and Prosthetics**
(antithrombogenic; **stents** with hybrid coating containing **polymer**, crosslinking agent, and therapeutic agent)

IT **Biocompatibility**
(hemocompatibility; **stents** with hybrid coating containing **polymer**, crosslinking agent, and therapeutic agent)

IT **Prosthetic materials and Prosthetics**
(**implants**; **stents** with hybrid coating containing **polymer**, crosslinking agent, and therapeutic agent)

IT **Artery, disease**
(**restenosis**, inhibition of; **stents** with hybrid coating containing **polymer**, crosslinking agent, and therapeutic agent)

IT Carboxylic acids, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(salts; **stents** with hybrid coating containing **polymer**, crosslinking agent, and therapeutic agent)

IT Anticoagulants
Crosslinking agents
(**stents** with hybrid coating containing **polymer**, crosslinking agent, and therapeutic agent)

IT Carboxylic acids, biological studies
Epoxy resins, biological studies
Polymers, biological studies
Polyurethanes, biological studies
Quaternary ammonium compounds, biological studies
Sulfonates
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**stents** with hybrid coating containing **polymer**,

crosslinking agent, and therapeutic agent)
IT **Medical goods**
(**stents**; **stents** with hybrid coating containing **polymer**, crosslinking agent, and therapeutic agent)
IT 151-56-4D, Aziridine, derivs., biological studies 9003-01-4, Poly(acrylic acid) 9005-49-6, Heparin, biological studies 25087-26-7, Poly(methacrylic acid) 29226-31-1, Poly(isocrotonic acid) **33069-62-4, Paclitaxel**
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**stents** with hybrid coating containing **polymer**, crosslinking agent, and therapeutic agent)
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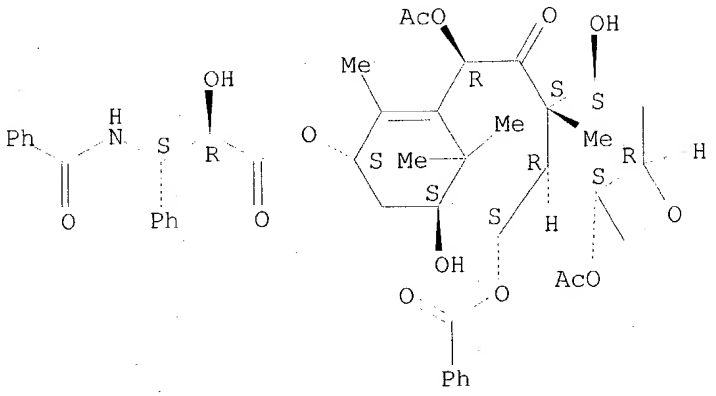
IT **33069-62-4, Paclitaxel**
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**stents** with hybrid coating containing **polymer**, crosslinking agent, and therapeutic agent)

RN 33069-62-4 HCAPLUS

CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L61 ANSWER 22 OF 30 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:75273 HCAPLUS
DN 134:136752
ED Entered STN: 01 Feb 2001
TI Hybrid coating for medical devices
IN Zhong, Sheng-ping
PA Boston Scientific Corporation, USA
SO U.S., 9 pp., Cont.-in-part of U.S. 5,869,127.
CODEN: USXXAM

DT Patent
LA English
IC ICM A61J003-00
ICS C08F283-00; A01N001-00
NCL 604265000
CC 63-7 (Pharmaceuticals)
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6179817	B1	20010130	US 1999-238707	19990128
	US 5702754	A	19971230	US 1995-392141	19950222
	US 5869127	A	19990209	US 1997-877825	19970618
PRAI	US 1995-392141	A2	19950222		
	US 1997-877825	A2	19970618		

AB Disclosed are hybrid coatings for implantable medical devices. Such coatings include a first layer of an aqueous dispersion or emulsion of an organic acid functional group containing **polymer**, a crosslinker and a therapeutic agent dispersed therein. The coating also includes a second layer of an aqueous solution or dispersion of an organic acid functional group-containing bio-active agent. The hybrid coatings are especially suited for preventing **restenosis** of endoprostheses by the combined **action** of the therapeutic agent and the bio-active agent. Methods of making and using devices coated with such compns. are also provided. A first coating composition containing polyetser-based aliphatic water-borne polyurethane containing carboxylic acid groups (NeoRez R981) 250, 0.5 % fluorad FC-129 stock solution 10, 34% NH4OH 4, Neocryl CX 100 crosslinker agent 20, and 20 % **Paclitaxel** stock solution 20 mL, and a second coating composition containing 1.2 % aqueous solution of sodium heparin 300 mL were applied on the surface of **stent** by spray coating sep., dried, and then put into a 50° vacuum oven for 3 h. The resulted coating has **controlled-releasable Paclitaxel** and covalently bond heparin on the surface.

ST prosthetic implant **biocompatible** coating polyurethane heparin

IT **Prosthetic materials and Prosthetics**
(antithrombogenic; **biocompatible**/bioactive hybrid coating for medical devices)

IT Angiogenesis inhibitors
Anti-inflammatory agents
Antibiotics
Anticoagulants
Antitumor agents
Antiviral agents
Ceramics
Genetics
Prosthetic materials and Prosthetics
(**biocompatible**/bioactive hybrid coating for medical devices)

IT Acrylic **polymers**, biological studies
Angiogenic factors
Epoxy resins, biological studies
Fluoropolymers, biological studies
Glass, biological studies
Glycosaminoglycans, biological studies
Integrins
Metals, biological studies
Natural rubber, biological studies
Polyamides, biological studies
Polycarbonates, biological studies
Polyesters, biological studies
Polyureas
Polyurethanes, biological studies

Silicone rubber, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**biocompatible**/bioactive hybrid coating for medical devices)

IT **Medical goods**
(**catheters; biocompatible**/bioactive hybrid coating for medical devices)

IT **Prosthetic materials and Prosthetics**
(**implants; biocompatible**/bioactive hybrid coating for medical devices)

IT Mitosis
(inhibitors; **biocompatible**/bioactive hybrid coating for medical devices)

IT Polysaccharides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(organic acid functional group-containing; **biocompatible**/bioactive hybrid coating for medical devices)

IT Polyethers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyester-; **biocompatible**/bioactive hybrid coating for medical devices)

IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyether-; **biocompatible**/bioactive hybrid coating for medical devices)

IT Aldehydes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyfunctional; **biocompatible**/bioactive hybrid coating for medical devices)

IT Cell cycle
(regulatory agents for; **biocompatible**/bioactive hybrid coating for medical devices)

IT **Medical goods**
(**stents; biocompatible**/bioactive hybrid coating for medical devices)

IT Medical goods
(wires; **biocompatible**/bioactive hybrid coating for medical devices)

IT 64265-57-2DP, **polymer** with urethane rubber 220482-45-1P
RL: IMF (Industrial manufacture); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**biocompatible**/bioactive hybrid coating for medical devices)

IT 3380-34-5, Triclosan 8001-27-2, Hirudin 9002-72-6, Growth hormone 9002-84-0, Polytetrafluoroethylene 9002-86-2, Polyvinyl chloride 9002-88-4, Polyethylene 9003-07-0, Polypropylene 9003-20-7, Polyvinyl acetate 9003-53-6, Polystyrene 9003-55-8 9004-61-9, Hyaluronic acid 9005-49-6, Heparin, biological studies 9007-28-7, Chondroitin sulfate 9041-08-1, Sodium heparin 24967-94-0, Dermatan sulfate 25038-59-9, Poly(ethylene terephthalate), biological studies **33069-62-4**, **Paclitaxel** 86090-08-6, Angiostatin 169799-44-4, Keratin sulfate 187888-07-9, Endostatin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**biocompatible**/bioactive hybrid coating for medical devices)

RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD

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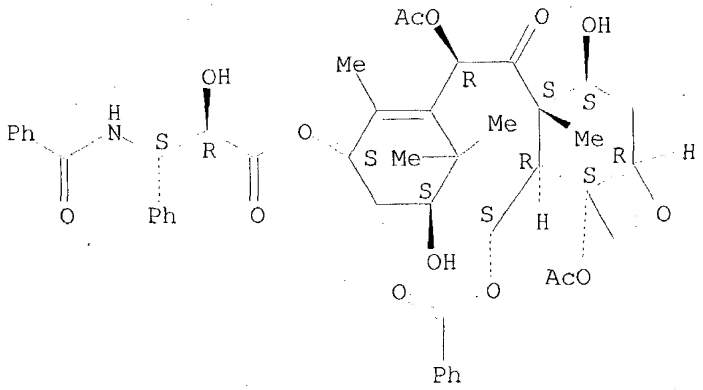
IT **33069-62-4, Paclitaxel**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**biocompatible**/bioactive hybrid coating for medical devices)

RN 33069-62-4 HCAPLUS
CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L61 ANSWER 23 OF 30 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:31277 HCAPLUS
DN 134:91188
ED Entered STN: 12 Jan 2001
TI Coated **stent** capable of releasing agents over time
IN Yang, Dachuan; Stanslaski, Joel L.; Wang, Lixiao; Smith, Scott R.

PA **Scimed Life Systems, Inc., USA**
SO PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61F002-06
ICS A61P035-00; A61K009-00
CC 63-7 (Pharmaceuticals)
Section cross-reference(s): 38
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001001890	A1	20010111	WO 2000-US40105	20000606
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2342866	AA	20010111	CA 2000-2342866	20000606
EP 1107707	A1	20010620	EP 2000-943431	20000606
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003503153	T2	20030128	JP 2001-507394	20000606
US 6569195	B2	20030527	US 2001-883870	20010618
PRAI US 1999-346975	A	19990702		
WO 2000-US40105	W	20000606		

AB A **stent** having a **polymeric** coating for **controllably releasing** an included active agent. The **polymeric** coating includes a blend of a first **polymeric** material, which if alone, would **release** the agent at a first, higher rate, and a second **polymeric** material, which if alone would **release** the agent at a second, lower rate over a longer time period. One **stent** coating utilizes a faster **releasing** hydrophilic **polymeric** material and a slower **releasing** hydrophobic material. One **stent** coating includes a blend of a faster **releasing** PLA-PEO **copolymer** and a slower **releasing** PLA-PCL **copolymer**. One active agent is **Taxol**. One use of the **taxol** delivering **stent** is to inhibit **restenosis** following **angioplasty**. A perspective view of a **stent** in accordance with an exemplary embodiment of the present invention is depicted (no data).

ST medical **stent** coating **polymer**

IT **Artery**
(**angioplasty**; coated **stent** capable of releasing agents over time)

IT **Polymers**, biological studies
Polyoxyalkylenes, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coated **stent** capable of releasing agents over time)

IT **Artery, disease**
(**restenosis**, inhibitor; coated **stent** capable of releasing agents over time)

IT **Medical goods**
(**stents**; coated **stent** capable of releasing agents over time)

IT 24980-41-4, Polycaprolactone 25248-42-4, Polycaprolactone 25322-68-3, Polyethylene oxide 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)]

26680-10-4, Polylactide
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coated **stent** capable of releasing agents over time)

IT **33069-62-4, Taxol 33069-62-4D, Paclitaxel**, analogs and derivs.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coated **stent** capable of releasing agents over time)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
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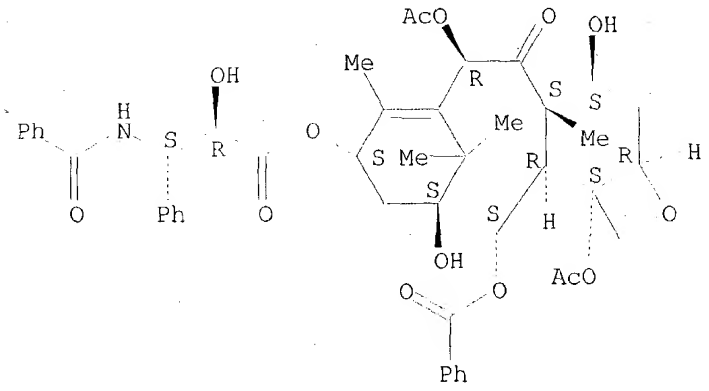
(3) Poly-Med Inc; EP 0737703 A 1996 HCAPLUS
(4) Scimed Life Systems Inc; WO 9856312 A 1998

IT **33069-62-4, Taxol 33069-62-4D, Paclitaxel**, analogs and derivs.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coated **stent** capable of releasing agents over time)

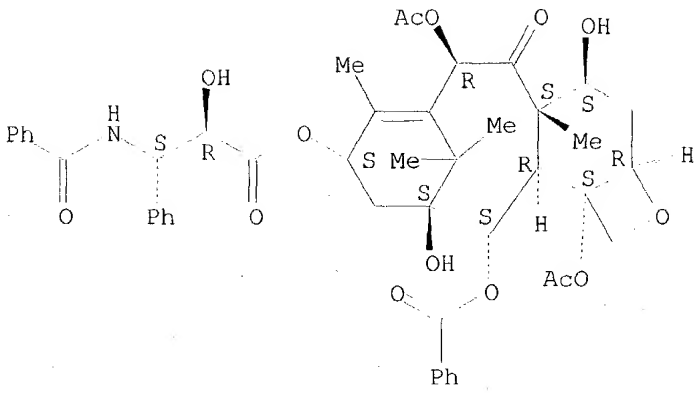
RN 33069-62-4 HCAPLUS
CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 33069-62-4 HCAPLUS
CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L61 ANSWER 24 OF 30 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:910988 HCAPLUS
DN 135:66113
ED Entered STN: 29 Dec 2000
TI Neointimal thickening after **stent** delivery of **paclitaxel** : change in composition and arrest of growth over six months
AU Drachman, Douglas E.; Edelman, Elazer R.; Seifert, Philip; Groothuis, Adam R.; Bornstein, Danielle A.; Kamath, Kalpana R.; Palasis, Maria; Yang, Dachuan; Nott, Sepideh H.; Rogers, Campbell
CS Department of Medicine, (Cardiac Catheterization Laboratory and Coronary Care Unit, Cardiovascular Division, Brigham and Women's Hospital), Harvard Medical School, Boston, MA, USA
SO Journal of the American College of Cardiology (2000), 36(7), 2325-2332
CODEN: JACCDI; ISSN: 0735-1097
PB Elsevier Science Inc.
DT Journal
LA English
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1
AB This study investigated the long-term effects of **stent**-based **paclitaxel** delivery on the extent, rate and composition of neointimal thickening after **stent** implantation. Stainless steel **stents** were implanted in the iliac arteries of rabbits after endothelial denudation. The **stents** were uncoated or coated with a thin layer of poly(lactide-co-E-caprolactone) **copolymer** alone or containing **paclitaxel**, 200 μg. **Paclitaxel release** in vitro followed 1st-order kinetics for two months. Tissue responses were examined 7, 28, 56 or 180 days after implantation. **Paclitaxel** had reduced intimal and medial cell proliferation 3-fold seven days after stenting and virtually eliminated later intimal thickening. Six months after stenting, long after drug **release** and **polymer** degradation were likely to be complete, neointimal area was two-fold lower with **paclitaxel-releasing** than with **control stents**. Tissue responses in **paclitaxel** -treated vessels included incomplete healing, few smooth muscle cells, late persistence of macrophages and dense fibrin with little collagen. Thus, poly(lactide-co-E-caprolactone) **copolymer**-coated **stents** permit **sustained paclitaxel** delivery in a manner that virtually abolishes neointimal hyperplasia for months after **stent** implantation, long after likely completion of drug delivery and **polymer** degradation
ST artery hyperplasia **paclitaxel stent** delivery polylactide **copolymer**
IT Artery
(iliac; neointimal thickening after **stent** delivery of

paclitaxel from polylactide-caprolactone **copolymer**)
IT Artery
(intima; neointimal thickening after **stent** delivery of **paclitaxel** from polylactide-caprolactone **copolymer**)
IT **Artery, disease**
(**restenosis**; neointimal thickening after **stent** delivery of **paclitaxel** from polylactide-caprolactone **copolymer**)
IT Drug delivery systems
(slow-release; artery neointimal thickening after **stent** delivery of **paclitaxel** from polylactide-caprolactone **copolymer**)
IT **Medical goods**
(**stents**; artery neointimal thickening after **stent** delivery of **paclitaxel** from polylactide-caprolactone **copolymer**)
IT **33069-62-4, Paclitaxel**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process)
(artery neointimal thickening after **stent** delivery of **paclitaxel** from polylactide-caprolactone **copolymer**)
IT 70524-20-8
RL: PEP (Physical, engineering or chemical process); POF (Polymer in formulation); PROC (Process); USES (Uses)
(artery neointimal thickening after **stent** delivery of **paclitaxel** from polylactide-caprolactone **copolymer**)
RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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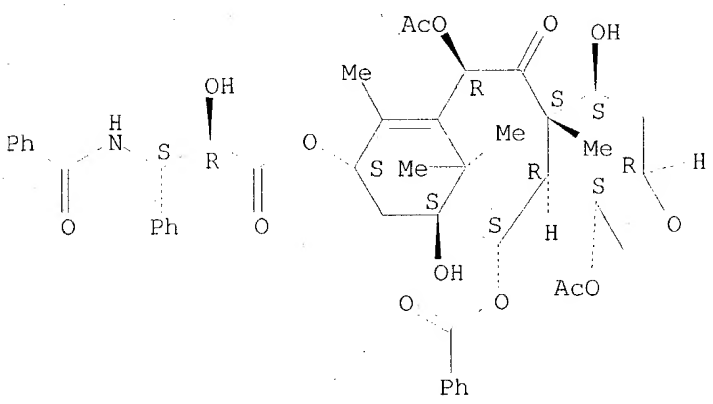
IT **33069-62-4, Paclitaxel**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process)
(artery neointimal thickening after **stent** delivery of **paclitaxel** from polylactide-caprolactone **copolymer**)

RN 33069-62-4 HCAPLUS

CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L61 ANSWER 25 OF 30 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2000:756571 HCAPLUS

DN 133:340283

ED Entered STN: 27 Oct 2000

TI Coating of medical devices with therapeutic agents, **polymers**, sugars and waxes using air suspension

IN Schwarz, Marlene; Miller, Kathleen; Kamath, Kalpana

PA **Scimed Life Systems, Inc., USA**

SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2

DT Patent

LA English

IC ICM A61L027-00

CC 63-7 (Pharmaceuticals)
Section cross-reference(s): 42

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000062830	A2	20001026	WO 2000-US10316	20000418
	WO 2000062830	A3	20001228		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

	US 6368658	B1	20020409	US 2000-551614	20000417
	EP 1171245	A2	20020116	EP 2000-926059	20000418

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

IE, SI, LT, LV, FI, RO
JP 2003524465 T2 20030819 JP 2000-611966 20000418
PRAI US 1999-293994 A 19990419
US 2000-551614 A 20000417
WO 2000-US10316 W 20000418

AB Methods and apparatuses for coating medical devices and the devices thereby produced are disclosed. In one embodiment, the invention includes a method comprising the steps of suspending the medical device in an air stream and introducing a coating material into the air stream such that the coating material is dispersed therein and coats at least a portion of the medical device. In another embodiment, the medical devices are suspended in an air stream and a coating apparatus coats at least a portion of the medical device with a coating material. The coating apparatus may include a device that utilizes any number of alternative coating techniques for coating the medical devices. This process is used to apply one or more coating materials, simultaneously or in sequence. In certain embodiments of the invention, the coating materials include therapeutic agents, **polymers**, sugars, waxes, or fats. By using air suspensions to coat medical devices, the methods of the present invention result in coatings having minimal defects and uniform thicknesses and mech. properties. Further, the methods of the present invention are time efficient and cost effective because they facilitate the coating of numerous medical devices in a single batch, resulting in numerous medical device units containing substantially the same coating. For example, coronary **stents** were coated with a solution containing 0.5-2.0% Elvax 40W and 0.05-0.6% **paclitaxel** in chloroform. The coating process resulted in **stents** coated with uniform coating layers in which **paclitaxel** was evenly distributed on each **stent** and substantially the same dose applied to every **stent** in the batch.

ST medical device coating air suspension; drug coating medical device; **polymer** coating medical device; sugar coating medical device; wax coating medical device

IT Urethane rubber, biological studies
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(Corethane 50D; coating of medical devices with therapeutic agents, **polymers**, sugars and waxes using air suspension)

IT Polysiloxanes, biological studies
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(MED 6605; coating of medical devices with therapeutic agents, **polymers**, sugars and waxes using air suspension)

IT Coating process
(UV deposition; coating of medical devices with therapeutic agents, **polymers**, sugars and waxes using air suspension)

IT Coating process
(air suspension; coating of medical devices with therapeutic agents, **polymers**, sugars and waxes using air suspension)

IT Quaternary ammonium compounds, biological studies
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(alkylbenzyldimethyl, chlorides; coating of medical devices with therapeutic agents, **polymers**, sugars and waxes using air suspension)

IT Filters
(blood; coating of medical devices with therapeutic agents, **polymers**, sugars and waxes using air suspension)

IT Polyesters, biological studies
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process);

USES (Uses)
(caprolactone-based; coating of medical devices with therapeutic agents, **polymers**, sugars and waxes using air suspension)

IT **Medical goods**
(**catheters**; coating of medical devices with therapeutic agents, **polymers**, sugars and waxes using air suspension)

IT Plates
Plates
(ceramic, fluid bed chambers; coating of medical devices with therapeutic agents, **polymers**, sugars and waxes using air suspension)

IT Fluidized beds
(chambers; coating of medical devices with therapeutic agents, **polymers**, sugars and waxes using air suspension)

IT Medical goods
(clips; coating of medical devices with therapeutic agents, **polymers**, sugars and waxes using air suspension)

IT **Polymers**, biological studies
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process);
USES (Uses)
(co-; coating of medical devices with therapeutic agents, **polymers**, sugars and waxes using air suspension)

IT Coating apparatus
Drug delivery systems
Electrodeposition
Electrostatic deposition
Genetic vectors
Medical goods
Needles (tools)
Polymerization
Solvents
Vapor deposition process
(coating of medical devices with therapeutic agents, **polymers**, sugars and waxes using air suspension)

IT Carbohydrates, biological studies
DNA
Ethylene-vinyl acetate rubber
Fats and Glyceridic oils, biological studies
Glycosaminoglycans, biological studies
Nucleic acids
Oligonucleotides
Peptides, biological studies
Polyamides, biological studies
Polyanhydrides
Polycarbonates, biological studies
Polyesters, biological studies
Polyethers, biological studies
Polymers, biological studies
Polyoxyalkylenes, biological studies
Polysaccharides, biological studies
Polysiloxanes, biological studies
Proteins, general, biological studies
Waxes
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process);
USES (Uses)
(coating of medical devices with therapeutic agents, **polymers**, sugars and waxes using air suspension)

IT Gelatins, biological studies
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process);
USES (Uses)

(crosslinked; coating of medical devices with therapeutic agents, **polymers**, sugars and waxes using air suspension)

IT Blood
(filters; coating of medical devices with therapeutic agents, **polymers**, sugars and waxes using air suspension)

IT Polyesters, biological studies
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(hydroxycarboxylic acid-based; coating of medical devices with therapeutic agents, **polymers**, sugars and waxes using air suspension)

IT Vapor deposition process
(ion plating; coating of medical devices with therapeutic agents, **polymers**, sugars and waxes using air suspension)

IT Polyesters, biological studies
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(lactic acid-based; coating of medical devices with therapeutic agents, **polymers**, sugars and waxes using air suspension)

IT Coating process
(microwave deposition; coating of medical devices with therapeutic agents, **polymers**, sugars and waxes using air suspension)

IT Polyethers, biological studies
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(ortho ester group-containing; coating of medical devices with therapeutic agents, **polymers**, sugars and waxes using air suspension)

IT Coating process
(plasma spraying; coating of medical devices with therapeutic agents, **polymers**, sugars and waxes using air suspension)

IT Ceramics
Ceramics
(plates, fluid bed chambers; coating of medical devices with therapeutic agents, **polymers**, sugars and waxes using air suspension)

IT Metals, uses
RL: DEV (Device component use); USES (Uses)
(plates, fluid bed chambers; coating of medical devices with therapeutic agents, **polymers**, sugars and waxes using air suspension)

IT Carboxylic acids, biological studies
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(polycarboxylic, **polymers**; coating of medical devices with therapeutic agents, **polymers**, sugars and waxes using air suspension)

IT Vinyl compounds, biological studies
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**polymers**; coating of medical devices with therapeutic agents, **polymers**, sugars and waxes using air suspension)

IT **Medical goods**
(**stents**, coronary; coating of medical devices with therapeutic agents, **polymers**, sugars and waxes using air suspension)

IT Coating process
(thermal evaporation; coating of medical devices with therapeutic agents, **polymers**, sugars and waxes using air suspension)

IT Coating process
(visible light deposition; coating of medical devices with therapeutic agents, **polymers**, sugars and waxes using air suspension)

IT 79-10-7D, Acrylic acid, esters, **polymers** 107-73-3, Phosphorylcholine 108-31-6D, Maleic anhydride, **polymers** 9002-88-4 9002-89-5, Polyvinyl alcohol 9003-01-4, Polyacrylic acid 9003-05-8, Polyacrylamide 9003-07-0, Polypropylene 9003-39-8, Polyvinylpyrrolidone 9003-53-6, Polystyrene 9004-34-6, Cellulose, biological studies 9004-65-3, Hydroxypropyl methyl cellulose 9005-49-6, Heparin, biological studies 15663-27-1, Cisplatin 24937-78-8, Elvax 40W 24980-41-4, Polycaprolactone 25248-42-4, Polycaprolactone 25316-40-9, Doxorubicin hydrochloride 25322-68-3 26009-03-0, Poly(glycolic acid) 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26100-51-6, Poly(lactic acid) 26124-68-5, Poly(glycolic acid) 26780-50-7, Poly(glycolide-co-lactide) 30280-72-9 **33069-62-4, Paclitaxel** 51110-01-1D, Somatostatin, analogs 99896-85-2 303176-49-0, Corethane 50D
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(coating of medical devices with therapeutic agents, **polymers**, sugars and waxes using air suspension)

IT 67-66-3, uses 109-99-9, uses 127-19-5, Dimethylacetamide
RL: NUU (Other use, unclassified); USES (Uses)
(coating of medical devices with therapeutic agents, **polymers**, sugars and waxes using air suspension)

IT 24937-78-8
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(ethylene-vinyl acetate rubber, coating of medical devices with therapeutic agents, **polymers**, sugars and waxes using air suspension)

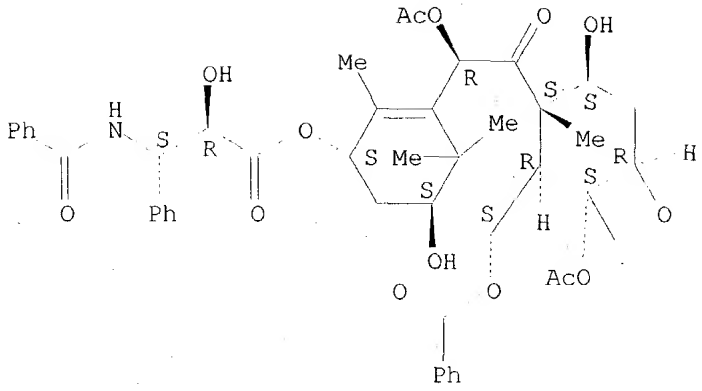
IT 111-30-8, Pentanedial
RL: NUU (Other use, unclassified); USES (Uses)
(gelatins crosslinked with; coating of medical devices with therapeutic agents, **polymers**, sugars and waxes using air suspension)

IT **33069-62-4, Paclitaxel**
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(coating of medical devices with therapeutic agents, **polymers**, sugars and waxes using air suspension)

RN 33069-62-4 HCAPLUS

CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L61 ANSWER 26 OF 30 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:658399 HCAPLUS
DN 133:242719
ED Entered STN: 20 Sep 2000
TI Surface treatment method for **stent polymeric** coating
IN Yang, Dachuan; Jacob, Carmen; Wang, Lixiao
PA **Scimed Life Systems, Inc., USA**
SO U.S., 8 pp.
CODEN: USXXAM
DT Patent
LA English
IC ICM B05D003-00
ICS B05D003-04
NCL 427335000
CC 63-7 (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6120847	A	20000919	US 1999-226930	19990108
PRAI	US 1999-226930		19990108		

AB A method is provided for eliminating surface imperfections on a medical device having a drug release coating including a therapeutic substance in a **polymeric** carrier disposed on at least a portion of the medical device. The medical device is preferably a **stent** including wire-like members interconnected to form struts with open interstices there-between. A therapeutic substance incorporated into a **polymeric** carrier is disposed on the surface of the **stent** through which process imperfections including **polymeric** fibers, **polymeric** particles or other **polymeric** surface aberrations or imperfections are formed. This imperfections are eliminated by contacting the **polymeric** coating with a vaporized solvent for a specified period of time.

ST drug release **stent polymer** coating surface treatment
IT Polyesters, biological studies
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(caprolactone-based; vaporized solvents in surface treatment of **polymeric stent** coatings for drug release)
IT Ethers, processes
RL: PEP (Physical, engineering or chemical process); PROC (Process)
(cyclic; vaporized solvents in surface treatment of **polymeric stent** coatings for drug release)
IT Hydrocarbons, processes
RL: PEP (Physical, engineering or chemical process); PROC (Process)

(halo; vaporized solvents in surface treatment of **polymeric stent** coatings for drug release)

IT Polyesters, biological studies
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(lactic acid-based; vaporized solvents in surface treatment of **polymeric stent** coatings for drug release)

IT Solvents
(organic, vaporizing; vaporized solvents in surface treatment of **polymeric stent** coatings for drug release)

IT Proliferation inhibition
(proliferation inhibitors; vaporized solvents in surface treatment of **polymeric stent** coatings for drug release)

IT **Medical goods**
(**stents**, endovascular; vaporized solvents in surface treatment of **polymeric stent** coatings for drug release)

IT Angiogenesis inhibitors
Anticoagulants
Cytotoxic agents
(vaporized solvents in surface treatment of **polymeric stent** coatings for drug release)

IT Polyesters, biological studies
Polymers, biological studies
Polyoxyalkylenes, biological studies
Polysiloxanes, biological studies
Polyurethanes, biological studies
Synthetic **polymeric** fibers, biological studies
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(vaporized solvents in surface treatment of **polymeric stent** coatings for drug release)

IT Alcohols, processes
Amides, processes
Hydrocarbons, processes
Polyethers, processes
RL: PEP (Physical, engineering or chemical process); PROC (Process)
(vaporized solvents in surface treatment of **polymeric stent** coatings for drug release)

IT Particles
(vaporized solvents in surface treatment of **polymeric stent** coatings for eliminating fibers and particles)

IT 24980-41-4, Polycaprolactone 25248-42-4, Polycaprolactone 25322-68-3, Polyethylene oxide 26009-03-0, Polyglycolic acid 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26100-51-6, Polylactic acid 26124-68-5, Polyglycolic acid
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(vaporized solvents in surface treatment of **polymeric stent** coatings for drug release)

IT 8001-27-2, Hirudin 9005-49-6, Heparin, biological studies **33069-62-4, Taxol** 55142-85-3, Ticlopidine
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vaporized solvents in surface treatment of **polymeric stent** coatings for drug release)

IT 71-43-2, Benzene, processes 71-43-2D, Benzene, alkyl-substituted derivs., processes 141-78-6, Ethyl acetate, processes
RL: PEP (Physical, engineering or chemical process); PROC (Process)
(vaporized solvents in surface treatment of **polymeric**

stent coatings for drug release)
RE.CNT 101 THERE ARE 101 CITED REFERENCES AVAILABLE FOR THIS RECORD
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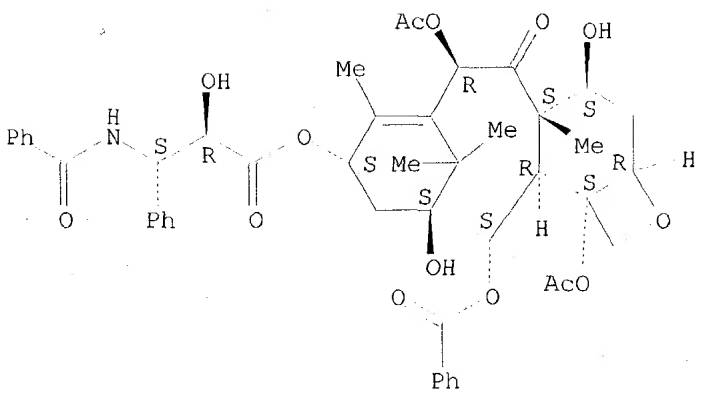
IT **33069-62-4, Taxol**
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vaporized solvents in surface treatment of **polymeric stent** coatings for drug release)

RN 33069-62-4 HCAPLUS

CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L61 ANSWER 27 OF 30 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:383988 HCAPLUS
DN 133:22475
ED Entered STN: 09 Jun 2000
TI **Stent** having drug crystals thereon
IN Palasis, Maria; Schwarz, Marlene
PA **Scimed Life Systems, Inc., USA**
SO PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K047-48
ICS A61L031-10; A61L029-10
CC 63-8 (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000032238	A1	20000608	WO 1999-US27279	19991117
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1135165	A1	20010926	EP 1999-961692	19991117
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRAI	US 1998-204255	A	19981203		
	WO 1999-US27279	W	19991117		

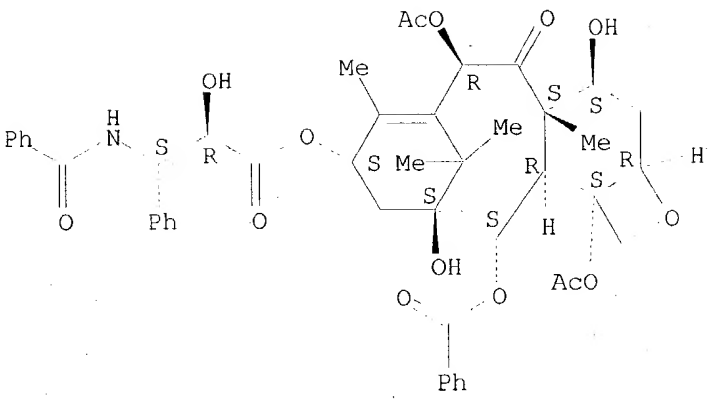
AB A medical device for insertion into a mammalian body, wherein the medical device has a crystalline therapeutic agent coated on it. Also provided is a method of delivering a therapeutic agent to a target location within a mammalian body. The method comprises the steps of placing crystals of the therapeutic agent on a medical device, and delivering the medical device to the target location. An example is given of formation of **paclitaxel** crystals from coated **stents** by exposure to a nonsolvent.

ST **stent** coating drug crystal; **paclitaxel** coating medical device

IT **Polymers**, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**biodegradable**; medical devices with drug coatings)
IT **Medical goods**
(**catheters**; medical devices with drug coatings)
IT Coating materials
Crystals
Medical goods
(medical devices with drug coatings)
IT Polyesters, biological studies
Polyurethanes, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medical devices with drug coatings)
IT **Medical goods**
(**stents**; medical devices with drug coatings)
IT **33069-62-4, Paclitaxel** 70524-20-8,
Caprolactone-lactide **copolymer**
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(medical devices with drug coatings)
RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Angiogenesis Tech Inc; WO 9503036 A 1995 HCAPLUS
(2) Farb, A; 70TH SCIENTIFIC SESSIONS OF THE AMERICAN HEART ASSOCIATION, Circulation 1997, V96(8 SUPPL), P1608
(3) Haehnel, I; 47TH ANNUAL SCIENTIFIC SESSION OF THE AMERICAN COLLEGE OF CARDIOLOGY, Journal of the American College of Cardiology 1998, V31(2 SUPPL A), P278A
(4) Haehnel, I; 48TH ANNUAL SCIENTIFIC SESSION OF THE AMERICAN COLLEGE OF CARDIOLOGY, Journal of the American College of Cardiology 1999, V33(2 SUPPL A), P222A
(5) Haehnel, I; XIXTH CONGRESS OF THE EUROPEAN SOCIETY OF CARDIOLOGY TOGETHER WITH THE 32ND ANNUAL GENERAL MEETING OF THE ASSOCIATION OF EUROPEAN PAEDIATRIC CARDIOLOGISTS, European Heart Journal 1997, V18(ABSTR SUPPL), P460
(6) Kornowski, R; 70TH SCIENTIFIC SESSIONS OF THE AMERICAN HEART ASSOCIATION, Circulation 1997, V96(8), P1341
(7) Manifold, D; DIGESTIVE DISEASE WEEK AND THE 99TH ANNUAL MEETING OF THE AMERICAN GASTROENTEROLOGICAL ASSOCIATION, PART 2, Gastroenterology 1998, V114(4), PA27
(8) Neorx Corp; WO 9843618 A 1998 HCAPLUS
(9) Reno, J; WO 9625176 A 1996 HCAPLUS
(10) Schierholz, J; BIOMATERIALS 1998, V19(22), P2065 HCAPLUS
(11) Voisard, R; XXTH CONGRESS OF THE EUROPEAN SOCIETY OF CARDIOLOGY, European Heart Journal 1998, V19(ABST SUPPL), P376
IT **33069-62-4, Paclitaxel**
RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(medical devices with drug coatings)
RN 33069-62-4 HCAPLUS
CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L61 ANSWER 28 OF 30 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:275378 HCAPLUS
DN 132:298866
ED Entered STN: 28 Apr 2000
TI Active substance-releasing **stents**, their production and use for prophylaxis of **restenosis**
PA Schering A.-G., Germany
SO Ger. Offen., 8 pp.
CODEN: GWXXBX
DT Patent
LA German
IC ICM A61F002-04
ICS A61L029-00; A61M036-12
CC 63-7 (Pharmaceuticals)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE 19849464	A1	20000427	DE 1998-19849464	19981021
PRAI DE 1998-19849464		19981021		

AB Metal or **polymer stents** are coated with a **polymer** to which cyclodextrin mols. are attached directly or via a linking mol. for binding an active substance. The active substance can be loaded on the cyclodextrin at any time from **stent** manufacture up to implantation, and a wide variety of active substances can be loaded onto **stents** in this manner for **sustained release** in vivo. Thus, a **stent** was dip-coated with a CHCl3 solution of an NH2 group-containing polyester-polyurethane to a thickness of 20 μm after drying, and then exposed to an acid chloride derivative of cyclodextrin. The coated **stent** was loaded with iloprost by immersion in an aqueous solution containing 10 ng-100 μg iloprost/mL, washed, and dried.

ST **stent** coating drug **sustained release**; cyclodextrin **polymer** conjugate **stent** coating

IT Lactams
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(N-vinyl, **polymers**, coatings; active substance-releasing **stents**, their production and use for prophylaxis of **restenosis**)

IT Polyamides, biological studies
Polyesters, biological studies
Polymers, biological studies
Polyoxyalkylenes, biological studies
Polysiloxanes, biological studies
Polysulfones, biological studies
Polyurethanes, biological studies

RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coatings; active substance-releasing **stents**, their production and use for prophylaxis of **restenosis**)

IT Dendritic **polymers**
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclodextrin conjugates; active substance-releasing **stents**, their production and use for prophylaxis of **restenosis**)

IT Peptides, biological studies
Polyamines
Polyamines
Polyesters, biological studies
Polyesters, biological studies
Polyethers, biological studies
Polyethers, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dendrimers, cyclodextrin conjugates; active substance-releasing **stents**, their production and use for prophylaxis of **restenosis**)

IT Drug delivery systems
(films, **sustained-release**; active substance-**releasing stents**, their production and use for prophylaxis of **restenosis**)

IT Dendritic **polymers**
Dendritic **polymers**
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyamines, cyclodextrin conjugates; active substance-releasing **stents**, their production and use for prophylaxis of **restenosis**)

IT Amines, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyamines, **nonpolymeric**, p-xylylene-, coatings; active substance-releasing **stents**, their production and use for prophylaxis of **restenosis**)

IT Dendritic **polymers**
Dendritic **polymers**
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyesters, cyclodextrin conjugates; active substance-releasing **stents**, their production and use for prophylaxis of **restenosis**)

IT Polyurethanes, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyether-, amino group-containing, coatings; active substance-releasing **stents**, their production and use for prophylaxis of **restenosis**)

IT Dendritic **polymers**
Dendritic **polymers**
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyethers, cyclodextrin conjugates; active substance-releasing **stents**, their production and use for prophylaxis of **restenosis**)

IT Ligands
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**polymer**-bound; active substance-releasing **stents**, their production and use for prophylaxis of **restenosis**)

IT Films
(**polymer**; active substance-releasing **stents**, their production and use for prophylaxis of **restenosis**)

IT Sulfonates
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**polymers**, coatings; active substance-releasing **stents**, their production and use for prophylaxis of **restenosis**)

IT **Artery, disease**
(**restenosis**; active substance-releasing **stents**, their production and use for prophylaxis of **restenosis**)

IT **Medical goods**
(**stents**; active substance-releasing **stents**, their production and use for prophylaxis of **restenosis**)

IT Metals, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**stents**; active substance-releasing **stents**, their production and use for prophylaxis of **restenosis**)

IT **33069-62-4**, **Taxol** 78919-13-8, Iloprost 152044-54-7, Epothilone B
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(active substance-releasing **stents**, their production and use for prophylaxis of **restenosis**)

IT 214261-08-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coatings; active substance-releasing **stents**, their production and use for prophylaxis of **restenosis**)

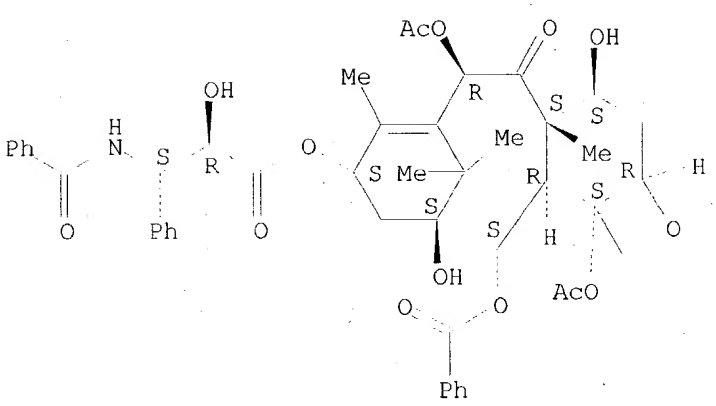
IT 88-12-0D, N-Vinyl-2-pyrrolidinone, **polymers** 502-86-3D, **polymers** with polyamines 3277-26-7 7440-21-3D, Silicon, organic compds., dendrimers, cyclodextrin conjugates, biological studies 7585-39-9D, β-Cyclodextrin, **polymer**-bound 7723-14-0D, Phosphorus, compds., dendrimers, cyclodextrin conjugates, biological studies 9002-86-2, Poly(vinyl chloride) 9002-88-4, Polyethylene 9003-05-8, Polyacrylamide 9011-14-7, Poly(methyl methacrylate) 10016-20-3D, α-Cyclodextrin, **polymer**-bound 12619-70-4D, Cyclodextrin, **polymer**-bound 17465-86-0D, γ-Cyclodextrin, **polymer**-bound 21982-30-9D, Hydroxymethyl methacrylate, **polymers** 25038-59-9, biological studies 25322-68-3, PEG 25322-69-4, Poly(propylene oxide)
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coatings; active substance-releasing **stents**, their production and use for prophylaxis of **restenosis**)

IT **33069-62-4**, **Taxol**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(active substance-releasing **stents**, their production and use for prophylaxis of **restenosis**)

RN 33069-62-4 HCAPLUS

CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



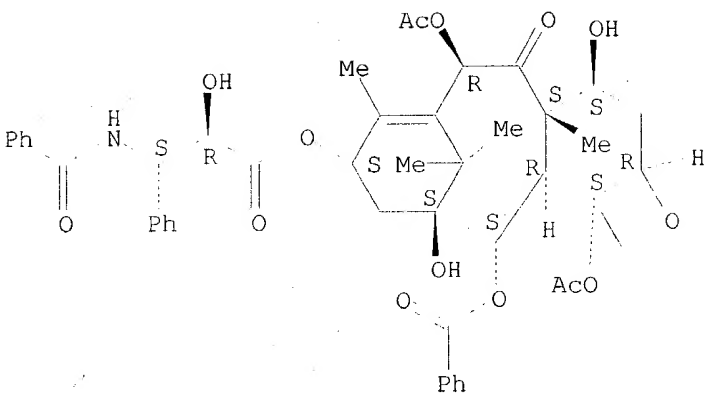
L61 ANSWER 29 OF 30 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:161180 HCAPLUS
DN 132:199080
ED Entered STN: 10 Mar 2000
TI Drug delivery device for **stent**
IN Yang, Dachuan; Wang, Lixiao
PA **Scimed Life Systems, Inc., USA**
SO PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61L031-08
ICS A61L031-16; A61L031-18; A61K051-12; A61F002-06
CC 63-6 (Pharmaceuticals)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000012147	A1	20000309	WO 1999-US19697	19990831
W: CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2338788	AA	20000309	CA 1999-2338788	19990831
EP 1119379	A1	20010801	EP 1999-946670	19990831
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRAI US 1998-145707	A	19980902		
WO 1999-US19697	W	19990831		

AB A device adapted for mounting on a **stent**, the device comprising a sheath being made of **polymeric** material that includes drugs such as radioactive agent(s) for delivery to an implant site. The sheath includes a main body of a generally tubular shape, and may include mounting means for attaching same to the **stent**. The device may have a slit, and may comprise a helical coil, a cylinder or any other suitable shape or design which fits a particular **stent**. The sheath may include a coating or coatings containing drugs, surgical adhesives or a combination thereof.
ST drug delivery device **stent**; **polymer** drug delivery device **stent**
IT Medical goods
Medical goods
(adhesives; drug delivery device for **stent**)
IT **Polymers**, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**biodegradable**; drug delivery device for **stent**)

IT Coating materials
Drug delivery systems
(drug delivery device for **stent**)
IT **Fluoropolymers**, biological studies
Gelatins, biological studies
Phenolic resins, biological studies
Polymers, biological studies
Polyoxyalkylenes, biological studies
Polyurethanes, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug delivery device for **stent**)
IT Fibrins
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(glues; drug delivery device for **stent**)
IT **Prosthetic materials and Prosthetics**
(**implants**; drug delivery device for **stent**)
IT Adhesives
Adhesives
(medical; drug delivery device for **stent**)
IT **Medical goods**
(**stents**; drug delivery device for **stent**)
IT 50-28-2, β-Estradiol, biological studies 51-21-8, 5-Fluorouracil 9002-84-0, PTFE 9003-39-8, PVp 9004-34-6, Cellulose, biological studies 9005-49-6, Heparin, biological studies 15421-84-8, Trapidil 15802-18-3D, Cyanoacrylic acid, esters, **polymers** 23288-49-5, Probucol 24969-11-7, Formaldehyde-resorcinol **copolymer** 25322-68-3, Polyethylene glycol **33069-62-4**, **Taxol** 53902-12-8, Tranilast 108736-35-2, Angiopeptin 127464-60-2, Vascular endothelial growth factor
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug delivery device for **stent**)
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Advanced Cardiovascular System; EP 0604022 A 1994 HCAPLUS
(2) Advanced Cardiovascular System; EP 0712615 A 1996
(3) Advanced Cardiovascular System; EP 0716836 A 1996
(4) Cook Inc; WO 9836784 A 1998 HCAPLUS
(5) Dayton, M; US 5578075 A 1996
(6) Reno John M; WO 9625176 A 1996 HCAPLUS
(7) Scimed Life Systems Inc; WO 9306792 A 1993
(8) Scimed Life Systems Inc; WO 9529647 A 1995 HCAPLUS
(9) Scott, N; US 5383928 A 1995
(10) Strecker Ernst Peter Dr Med Pr; EP 0578998 A 1994
IT **33069-62-4**, **Taxol**
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug delivery device for **stent**)
RN 33069-62-4 HCAPLUS
CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L61 ANSWER 30 OF 30 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:753125 HCAPLUS
DN 131:356143
ED Entered STN: 26 Nov 1999
TI Porous implant containing therapeutically useful compositions
IN Weadock, Kevin
PA **Scimed Life Systems, Inc., USA**
SO PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61L027-00
CC 63-6 (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9959648	A1	19991125	WO 1999-US10901	19990518
	W: AU, CA, JP				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2333172	AA	19991125	CA 1999-2333172	19990518
	AU 9939994	A1	19991206	AU 1999-39994	19990518
	EP 1079871	A1	20010307	EP 1999-923162	19990518
	R: DE, FR, GB, NL, IE				
	US 6210436	B1	20010403	US 1999-325024	19990603
	US 6447542	B1	20020910	US 2000-613201	20000711
PRAI	US 1998-80736	A	19980518		
	WO 1999-US10901	W	19990518		
	US 1999-325024	A3	19990603		

AB An implantable prosthesis includes a porous **polymeric** member having pores present in its wall structure wherein these pores contain a variety of therapeutically useful compns. including collagen, genetically altered cells and piezoelec. materials. A process of preparing such a prosthesis is also disclosed.
ST prosthetic **polymer** implant therapeutic impregnation
IT Antibiotics
(aminoglycoside; porous **polymeric** implants containing therapeutically useful compns.)
IT Hydrocarbons, biological studies
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(fluoro; porous **polymeric** implants containing therapeutically useful compns.)
IT **Drug delivery systems**
Prosthetic materials and Prosthetics

(**implants**; porous **polymeric implants** containing therapeutically useful compns.)

IT Mitosis
(inhibitors; porous **polymeric** implants containing therapeutically useful compns.)

IT Vapor deposition process
(ion plating; porous **polymeric** implants containing therapeutically useful compns.)

IT Polyethers, biological studies
Polyethers, biological studies
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(polyester-; porous **polymeric** implants containing therapeutically useful compns.)

IT Polyesters, biological studies
Polyesters, biological studies
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(polyether-; porous **polymeric** implants containing therapeutically useful compns.)

IT Aldehydes, biological studies
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(polyfunctional; porous **polymeric** implants containing therapeutically useful compns.)

IT Alkylating agents, biological
Angiogenesis inhibitors
Anti-inflammatory agents
Antibiotics
Anticoagulants
Antitumor agents
Antiviral agents
Ferroelectric materials
Piezoelectric materials
(porous **polymeric** implants containing therapeutically useful compns.)

IT Alkaloids, biological studies
Angiogenic factors
Collagens, biological studies
Enzymes, biological studies
Fluoropolymers, biological studies
Genetic element
Hormones, animal, biological studies
Interferons
Natural rubber, biological studies
Polyamides, biological studies
Polycarbonates, biological studies
Polyesters, biological studies
Polyesters, biological studies
Polyureas
Polyurethanes, biological studies
Proteins, general, biological studies
Silicone rubber, biological studies
Sulfonamides
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(porous **polymeric** implants containing therapeutically useful compns.)

IT Cell cycle
(regulators; porous **polymeric** implants containing therapeutically useful compns.)

IT 50-18-0, Cyclophosphamide 50-44-2, 6-Mercaptopurine 51-21-8, 5-Fluorouracil 51-75-2, Mechlorethamine 54-42-2, Idoxuridine

56-75-7, Chloramphenicol 57-22-7, Vincristine 59-05-2, Methotrexate 60-54-8, Tetracycline 70-00-8, Trifluridine 114-07-8, Erythromycin 147-94-4, Cytarabine 148-82-3, Melphalan 154-21-2, Lincomycin 154-93-8, Carmustine 305-03-3, Chlorambucil 768-94-5, Tricyclo[3.3.1.13,7]decan-1-amine 865-21-4, Vinblastine 1404-00-8, Mitomycin 1404-90-6, Vancomycin 1406-05-9, Penicillin 1406-11-7, **Polymyxin** 3778-73-2, Ifosfamide 4428-95-9, Foscarnet 5536-17-4, Vidarabine 8001-27-2, Hirudin 9002-01-1, Streptokinase 9002-72-6, Growth hormone 9002-84-0 9002-86-2, Polyvinyl chloride 9002-88-4, Polyethylene 9003-07-0, Polypropylene 9003-20-7, Polyvinyl acetate 9003-24-1, Vinylidene cyanide-vinyl acetate **copolymer** 9003-53-6, Polystyrene 9003-55-8 9004-61-9, Hyaluronic acid 9005-49-6, Heparin, biological studies 9007-28-7, Chondroitin sulfate 9015-68-3, Asparaginase 9039-53-6, Urokinase 9050-30-0, Heparan sulfate 9056-36-4, Keratan sulfate 10043-66-0, Iodine (131), biological studies 10098-91-6, Yttrium(90), biological studies 10540-29-1, Tamoxifen 11056-06-7, Bleomycin 11111-12-9, Cephalosporin 12587-46-1, α-Particle 12587-47-2, β-Particle 13010-47-4, Lomustine 13311-84-7, Flutamide 13392-28-4, Rimantadine 14596-37-3, Phosphorus(32), biological studies 15663-27-1, Cisplatin 18323-44-9, Clindamycin 20830-81-3, Daunomycin 23214-92-8, Doxorubicin 24937-79-9 24967-94-0, Dermatan sulfate 24980-41-4, Poly(ε-caprolactone) 24981-14-4, Polyvinylfluoride 25014-27-1, Poly(γ-benzylglutamate) 25035-04-5, Nylon 11 25038-53-3, Poly(γ-benzylglutamate) 25038-59-9, biological studies 25248-42-4, Poly[oxy(1-oxo-1,6-hexanediyl)] 25587-80-8 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26063-00-3, Polyhydroxybutyrate 26100-51-6, Polylactic acid 26744-04-7 28960-88-5, Vinylidene fluoride-trifluoroethylene **copolymer** 30516-87-1, Zidovudine **33069-62-4, Paclitaxel** 33419-42-0, Etoposide 35561-98-9, Poly(p-methylbenzyl L-glutamate) 36791-04-5, Ribavirin 59277-89-3, Acyclovir 82410-32-0, Ganciclovir 86090-08-6, Angiostatin 114977-28-5, Docetaxel 139639-23-9, Tissue plasminogen activator 187888-07-9, Endostatin

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(porous **polymeric** implants containing therapeutically useful compns.)

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Beatrice, H; WO 9608149 A 1996 HCAPLUS
(2) Darouiche, R; US 5624704 A 1997 HCAPLUS
(3) Kadletz, M; THORAC CARDIOVASC SURGEON 1987, V35, P143
(4) Kevin, W; US 5665114 A 1997
(5) Medtronic Inc; EP 0596615 A 1994 HCAPLUS
(6) Michel, H; WO 9424298 A 1994 HCAPLUS
(7) Patrick, A; US 5030225 A 1991

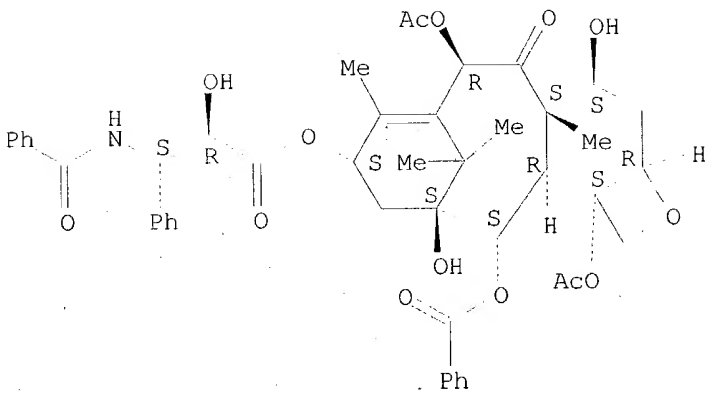
IT **33069-62-4, Paclitaxel**

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(porous **polymeric** implants containing therapeutically useful compns.)

RN 33069-62-4 HCAPLUS

CN Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-, (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-6,12b-bis(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-4,11-dihydroxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1H-cyclodeca[3,4]benz[1,2-b]oxet-9-yl ester, (αR,βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



=> => fil medline
FILE 'MEDLINE' ENTERED AT 09:39:18 ON 20 JAN 2004

FILE LAST UPDATED: 17 JAN 2004 (20040117/UP). FILE COVERS 1958 TO DATE.

On December 14, 2003, the 2004 MeSH terms were loaded. See HELP RLOAD for details.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2004 vocabulary. See http://www.nlm.nih.gov/mesh/ and http:\\www.nih.gov/pubs/yechbull/nd03/nd03_mesh.html for a description on changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d l89 all tot

L89 ANSWER 1 OF 17 MEDLINE on STN
AN 2003576190 MEDLINE
DN PubMed ID: 14658445
TI [Are drug-coated **stents** too expensive?].
Sind medikamentenbeschichtete **Stents** zu teuer?.
AU Kaulen Hildegard
SO Deutsche medizinische Wochenschrift, (2003 Nov 21) 128 (47) 2466.
Journal code: 0006723. ISSN: 0012-0472.
CY Germany: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA German
FS Priority Journals
EM 200312
ED Entered STN: 20031216
Last Updated on STN: 20031216
Entered Medline: 20031212
CT Check Tags: Human
*Antineoplastic Agents: AD, administration & dosage
Antineoplastic Agents: EC, economics
Cell Division: DE, drug effects
***Coronary Stenosis: TH, therapy**
Delayed-Action Preparations
Germany
*Immunosuppressive Agents: AD, administration & dosage
Immunosuppressive Agents: EC, economics
Paclitaxel: AD, administration & dosage

Paclitaxel: EC, economics
Recurrence: PC, prevention & control
Sirolimus: AD, administration & dosage
Sirolimus: EC, economics
Stents: CL, classification
***Stents: EC, economics**
RN **33069-62-4 (Paclitaxel)**; 53123-88-9 (Sirolimus)
CN 0 (Antineoplastic Agents); 0 (Delayed-Action Preparations); 0 (Immunosuppressive Agents)

L89 ANSWER 2 OF 17 MEDLINE on STN
AN 2003507691 MEDLINE
DN 22944420 PubMed ID: 14584494
TI Drug-eluting **stents** substantially lower rate of **restenosis**.
AU Rollins Gina
SO Rep Med Guidel Outcomes Res, (2003 Oct 17) 14 (20) 7-9.
Journal code: 9106372. ISSN: 1050-5636.
CY United States
DT News Announcement
LA English
FS Health Technology
EM 200310
ED Entered STN: 20031031
Last Updated on STN: 20031101
Entered Medline: 20031031
CT Check Tags: Comparative Study; Human
***Coronary Restenosis: DT, drug therapy**
Coronary Restenosis: EC, economics
Coronary Restenosis: EP, epidemiology
Coronary Restenosis: PC, prevention & control
Costs and Cost Analysis
Diffusion of Innovation
***Paclitaxel: TU, therapeutic use**
Risk Assessment
*Sirolimus: TU, therapeutic use
***Stents**
Stents: EC, economics
Treatment Outcome
United States
United States Food and Drug Administration
RN **33069-62-4 (Paclitaxel)**; 53123-88-9 (Sirolimus)

L89 ANSWER 3 OF 17 MEDLINE on STN
AN 2003433020 MEDLINE
DN PubMed ID: 12974266
TI [Clinical trial of **paclitaxel**-eluting **stents**. Results of ASPECT].
Aziatskoe klinicheskoe issledovanie **stenta**, pokrytogo paklitakselem.
AU Liakishev A A
SO Kardiologiia, (2003) 43 (6) 72.
Journal code: 0376351. ISSN: 0022-9040.
CY Russia: Russian Federation
DT (CLINICAL TRIAL)
(MULTICENTER STUDY)
News Announcement
(RANDOMIZED CONTROLLED TRIAL)
LA Russian
FS Priority Journals
EM 200312
ED Entered STN: 20030917
Last Updated on STN: 20031224

Entered Medline: 20031223
CT China
Coronary Arteriosclerosis: SU, surgery
***Graft Occlusion, Vascular: PC, prevention & control**
Korea
***Paclitaxel**
Paclitaxel: AE, adverse effects
***Stents**
Stents: AE, adverse effects
Treatment Outcome
RN **33069-62-4 (Paclitaxel)**

L89 ANSWER 4 OF 17 MEDLINE on STN
AN 2003366025 MEDLINE
DN 22781892 PubMed ID: 12900499
TI **Paclitaxel**-eluting **stents** come out winners again.
CM Comment on: Circulation. 2003 Aug 5;108(5):530-5
AU SoRelle Ruth
SO CIRCULATION, (2003 Aug 5) 108 (5) e9008-9.
Journal code: 0147763. ISSN: 1524-4539.
CY United States
DT Commentary
News Announcement
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200309
ED Entered STN: 20030806
Last Updated on STN: 20030916
Entered Medline: 20030915
CT Check Tags: Human
Delayed-Action Preparations
Drug Delivery Systems
Drug Implants
*Exercise: PH, physiology
***Graft Occlusion, Vascular: PC, prevention & control**
Multicenter Studies
Oxidative Stress
Oxygen Consumption
***Paclitaxel: AD, administration & dosage**
Randomized Controlled Trials
***Stents**
*Vasodilation: PH, physiology
RN **33069-62-4 (Paclitaxel)**
CN 0 (Delayed-Action Preparations); 0 (Drug Implants)

L89 ANSWER 5 OF 17 MEDLINE on STN
AN 2003214445 MEDLINE
DN 22620798 PubMed ID: 12735042
TI Prevention of postangioplasty **restenosis.**
AU Kitai Tamaki; Ishiwata Sugao; Yamaguchi Tetsu
CS Cardiovascular Center, Toranomon Hospital.
SO NIPPON RINSHO. JAPANESE JOURNAL OF CLINICAL MEDICINE, (2003 Apr) 61 Suppl 4 627-31. Ref: 15
Journal code: 0420546. ISSN: 0047-1852.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA Japanese
FS Priority Journals
EM 200307
ED Entered STN: 20030509
Last Updated on STN: 20030730

Entered Medline: 20030729
CT Check Tags: Human
***Angioplasty, Transluminal, Percutaneous Coronary: AE, adverse effects**
Anthranilic Acids: TU, therapeutic use
Atherectomy, Coronary
Clinical Trials
Coated Materials, Biocompatible
Coronary Disease: TH, therapy
***Coronary Restenosis: ET, etiology**
Coronary Restenosis: PA, pathology
***Coronary Restenosis: PC, prevention & control**
Paclitaxel: AD, administration & dosage
Probucol: TU, therapeutic use
Radiotherapy
Sirolimus: AD, administration & dosage
Stents
Trapidil: TU, therapeutic use
RN 15421-84-8 (Trapidil); 23288-49-5 (Probucol); **33069-62-4 (Paclitaxel)**; 53123-88-9 (Sirolimus); 53902-12-8 (Tranilast)
CN 0 (Anthranilic Acids); 0 (Coated Materials, Biocompatible)

L89 ANSWER 6 OF 17 MEDLINE on STN
AN 2003201301 MEDLINE
DN 22606683 PubMed ID: 12722545
TI [Use of coronary **stents**].
De l'usage des endoprotheses coronaires.
AU Chevalier B; Eltchaninoff H; Blanchard D; Finet G; Bedossa M; Corcos T; Fourrier J L; Hanssen M; Lefevre T; Puel J
CS Societe francaise de cardiologie, 15, rue Cels, 75014 Paris.
SO ARCHIVES DES MALADIES DU COEUR ET DES VAISSEAUX, (2003 Mar) 96 (3) 163-74.
Ref: 77
Journal code: 0406011. ISSN: 0003-9683.
CY France
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA French
FS Priority Journals
EM 200307
ED Entered STN: 20030501
Last Updated on STN: 20030716
Entered Medline: 20030715
CT Check Tags: Human
Angiogenesis Inhibitors: AD, administration & dosage
***Angioplasty, Transluminal, Percutaneous Coronary: IS, instrumentation**
Angioplasty, Transluminal, Percutaneous Coronary: MT, methods
Clinical Trials
Coronary Restenosis: PC, prevention & control
Coronary Vessels: PA, pathology
Coronary Vessels: SU, surgery
Paclitaxel: AD, administration & dosage
***Stents**
RN **33069-62-4 (Paclitaxel)**
CN 0 (Angiogenesis Inhibitors)

L89 ANSWER 7 OF 17 MEDLINE on STN
AN 2003162908 MEDLINE
DN 22524330 PubMed ID: 12637894
TI Drug-eluting **stents**.
AU Anonymous
SO MEDICAL LETTER ON DRUGS AND THERAPEUTICS, (2003 Mar 17) 45 (1152) 23-4.

Journal code: 2985240R. ISSN: 0025-732X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200304
ED Entered STN: 20030409
Last Updated on STN: 20030417
Entered Medline: 20030415
CT Coated Materials, Biocompatible: TU, therapeutic use
***Coronary Restenosis: PC, prevention & control**
*Drug Delivery Systems
Fees, Pharmaceutical
Paclitaxel: TU, therapeutic use
***Prosthesis Implantation: MT, methods**
Sirolimus: TU, therapeutic use
***Stents**
Stents: ST, standards
RN **33069-62-4 (Paclitaxel)**; 53123-88-9 (Sirolimus)
CN 0 (Coated Materials, Biocompatible)

L89 ANSWER 8 OF 17 MEDLINE on STN
AN 2003020754 MEDLINE
DN 22415179 PubMed ID: 12527687
TI In-**stent** stenosis: pathology and implications for the development of drug eluting **stents**.
AU Bennett Martin R
CS Addenbrooke's Centre for Clinical Investigation, Box 110, Addenbrooke's Hospital, Cambridge CB2 2QQ, UK.. mrb@mole.bio.cam.ac.uk
SO HEART, (2003 Feb) 89 (2) 218-24. Ref: 20
Journal code: 9602087. ISSN: 1468-201X.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200303
ED Entered STN: 20030116
Last Updated on STN: 20030308
Entered Medline: 20030307
CT Check Tags: Human
Angiogenesis Inhibitors: AD, administration & dosage
Brachytherapy: MT, methods
Coronary Restenosis: PA, pathology
***Coronary Restenosis: PC, prevention & control**
*Drug Implants
Drug Implants: AE, adverse effects
***Graft Occlusion, Vascular: PC, prevention & control**
Immunosuppressive Agents: AD, administration & dosage
Paclitaxel: AD, administration & dosage
Sirolimus: AD, administration & dosage
***Stents**
RN **33069-62-4 (Paclitaxel)**; 53123-88-9 (Sirolimus)
CN 0 (Angiogenesis Inhibitors); 0 (Drug Implants); 0 (Immunosuppressive Agents)

L89 ANSWER 9 OF 17 MEDLINE on STN
AN 2002705892 MEDLINE
DN 22355436 PubMed ID: 12468460
TI Drug eluting coronary **stents**.
AU Jenkins N P; Prendergast B D; Thomas M
SO BMJ (CLINICAL RESEARCH ED.), (2002 Dec 7) 325 (7376) 1315-6.

Journal code: 8900488. ISSN: 1468-5833.
CY England: United Kingdom
DT Editorial
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200212
ED Entered STN: 20021217
Last Updated on STN: 20021218
Entered Medline: 20021217
CT Check Tags: Human; Support, Non-U.S. Gov't
Antineoplastic Agents: AD, administration & dosage
***Coronary Restenosis: PC, prevention & control**
Drug Implants
Paclitaxel: AD, administration & dosage
Randomized Controlled Trials
Sirolimus: AD, administration & dosage
***Stents**
RN **33069-62-4 (Paclitaxel)**; 53123-88-9 (Sirolimus)
CN 0 (Antineoplastic Agents); 0 (Drug Implants)

L89 ANSWER 10 OF 17 MEDLINE on STN
AN 2002371290 MEDLINE
DN 22112192 PubMed ID: 12116826
TI Modern strategies to prevent coronary **restenosis.**
AU Chieffo Alaide; Stankovic Goran; Colombo Antonio
CS Laboratory of Interventional Cardiology, EMO Centro Cuore Columbus, Fondazione Centro San Raffaele del Monte Tabor, Milan, Italy.
SO ITALIAN HEART JOURNAL, (2002 Jun) 3 Suppl 4 9S-15S. Ref: 49
Journal code: 100909716. ISSN: 1129-471X.
CY Italy
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200302
ED Entered STN: 20020716
Last Updated on STN: 20030214
Entered Medline: 20030213
CT Check Tags: Human
Angioplasty, Transluminal, Percutaneous Coronary
Antineoplastic Agents: TU, therapeutic use
Atherectomy, Coronary
Brachytherapy
*Coronary Arteriosclerosis: TH, therapy
***Coronary Restenosis: PC, prevention & control**
Paclitaxel: TU, therapeutic use
Sirolimus: TU, therapeutic use
***Stents**
Ultrasonography, Interventional
RN **33069-62-4 (Paclitaxel)**; 53123-88-9 (Sirolimus)
CN 0 (Antineoplastic Agents)

L89 ANSWER 11 OF 17 MEDLINE on STN
AN 2002343491 MEDLINE
DN 22080947 PubMed ID: 12086391
TI Drug-eluting **stents** in the treatment of atherosclerotic coronary heart disease.
AU Lemos Pedro A; Regar Evelyn; Serruys Patrick W
CS Department of Cardiology, Thoraxcentre, Erasmus Medical Centre, Rotterdam.
SO INDIAN HEART JOURNAL, (2002 Mar-Apr) 54 (2) 212-6. Ref: 47
Journal code: 0374675. ISSN: 0019-4832.
CY India

DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200207
ED Entered STN: 20020628
Last Updated on STN: 20020726
Entered Medline: 20020725
CT Check Tags: Human
Antineoplastic Agents: TU, therapeutic use
Coronary Arteriosclerosis: CO, complications
*Coronary Arteriosclerosis: DT, drug therapy
Coronary Arteriosclerosis: TH, therapy
Coronary Restenosis: ET, etiology
***Coronary Restenosis: PC, prevention & control**
Dactinomycin: TU, therapeutic use
Drug Implants
Paclitaxel: TU, therapeutic use
Sirolimus: TU, therapeutic use
***Stents**
Treatment Outcome
RN **33069-62-4 (Paclitaxel)**; 50-76-0 (Dactinomycin); 53123-88-9 (Sirolimus)
CN 0 (Antineoplastic Agents); 0 (Drug Implants)

L89 ANSWER 12 OF 17 MEDLINE on STN
AN 2002136051 MEDLINE
DN 21685797 PubMed ID: 11827678
TI New tools for prevention of **restenosis** could decrease the "oculo-**stento**" reflex.
CM Comment on: Cardiovasc Res. 2002 Feb 1;53(2):481-6
AU Sturek Michael; Reddy Hanumanth K
SO CARDIOVASCULAR RESEARCH, (2002 Feb 1) 53 (2) 292-3.
Journal code: 0077427. ISSN: 0008-6363.
CY Netherlands
DT Commentary
Editorial
LA English
FS Priority Journals
EM 200203
ED Entered STN: 20020302
Last Updated on STN: 20020312
Entered Medline: 20020311
CT Check Tags: Animal; Human
Angioplasty, Transluminal, Percutaneous Coronary
*Antibiotics, Antineoplastic: TU, therapeutic use
Antineoplastic Agents: TU, therapeutic use
***Coronary Restenosis: PC, prevention & control**
Coronary Stenosis: TH, therapy
Drug Implants
Injections, Intra-Arterial
Models, Animal
***Paclitaxel: AA, analogs & derivatives**
Paclitaxel: TU, therapeutic use
Rabbits
Rats
*Sirolimus: TU, therapeutic use
***Stents**
RN 114977-28-5 (docetaxel); **33069-62-4 (Paclitaxel)**; 53123-88-9 (Sirolimus)
CN 0 (Antibiotics, Antineoplastic); 0 (Antineoplastic Agents); 0 (Drug Implants)

L89 ANSWER 13 OF 17 MEDLINE on STN
AN 2002134402 MEDLINE
DN 21858469 PubMed ID: 11870953
TI Drug-eluting **stents** for the prevention of **restenosis**: in quest for the Holy Grail.
AU Hiatt Bonnie L; Ikeno Fumaiki; Yeung Alan C; Carter Andrew J
CS Stanford University Medical Center, Stanford, California.
SO CATHETERIZATION AND CARDIOVASCULAR INTERVENTIONS, (2002 Mar) 55 (3) 409-17.
Journal code: 100884139. ISSN: 1522-1946.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200204
ED Entered STN: 20020301
Last Updated on STN: 20020501
Entered Medline: 20020430
CT Check Tags: Animal; Human
Cell Division: DE, drug effects
Clinical Trials
*Coated Materials, Biocompatible
Coronary Restenosis: ET, etiology
***Coronary Restenosis: PC, prevention & control**
Dactinomycin: AD, administration & dosage
Depression, Chemical
*Infusion Pumps, Implantable
Muscle, Smooth, Vascular: CY, cytology
Paclitaxel: AD, administration & dosage
Paclitaxel: PD, pharmacology
Sirolimus: AD, administration & dosage
Sirolimus: PD, pharmacology
***Stents**
Stents: AE, adverse effects
RN **33069-62-4 (Paclitaxel)**; 50-76-0 (Dactinomycin); 53123-88-9 (Sirolimus)
CN 0 (Coated Materials, Biocompatible)

L89 ANSWER 14 OF 17 MEDLINE on STN
AN 2002134401 MEDLINE
DN 21858468 PubMed ID: 11870952
TI **Stent**-based antirestenotic coatings (sirolimus/**paclitaxel**).
AU Oberhoff Martin; Herdeg Christian; Baumbach Andreas; Karsch Karl R
CS Bristol Heart Institute, University of Bristol, Bristol, U.K..
martin.oberhoff@bristol.ac.uk
SO CATHETERIZATION AND CARDIOVASCULAR INTERVENTIONS, (2002 Mar) 55 (3) 404-8.
Ref: 49
Journal code: 100884139. ISSN: 1522-1946.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200204
ED Entered STN: 20020301
Last Updated on STN: 20020501
Entered Medline: 20020430
CT Check Tags: Animal; Human
*Antineoplastic Agents, Phytogenic: AD, administration & dosage
Antineoplastic Agents, Phytogenic: PD, pharmacology

Cell Division: DE, drug effects
Clinical Trials
*Coated Materials, Biocompatible
Coronary Restenosis: ET, etiology
***Coronary Restenosis: PC, prevention & control**
Depression, Chemical
*Immunosuppressive Agents: AD, administration & dosage
Immunosuppressive Agents: PD, pharmacology
*Infusion Pumps, Implantable
Muscle, Smooth, Vascular: CY, cytology
***Paclitaxel: AD, administration & dosage**
Paclitaxel: PD, pharmacology
*Sirolimus: AD, administration & dosage
Sirolimus: PD, pharmacology
***Stents**
Stents: AE, adverse effects
RN **33069-62-4 (Paclitaxel)**; 53123-88-9 (Sirolimus)
CN 0 (Antineoplastic Agents, Phytogenic); 0 (Coated Materials, Biocompatible); 0 (Immunosuppressive Agents)

L89 ANSWER 15 OF 17 MEDLINE on STN
AN 2002103488 MEDLINE
DN 21823108 PubMed ID: 11835023
TI Highlights from the American Heart Association annual scientific sessions 2001: November 11 to 14, 2001.
AU Kandzari David E; Kay Joseph; O'Shea J Conor; Trichon Benjamin H; Donahue Mark; Liao Lawrence; Rao Sunil V
CS Duke Clinical Research Institute, Durham, NC 27715, USA.
SO AMERICAN HEART JOURNAL, (2002 Feb) 143 (2) 217-28.
Journal code: 0370465. ISSN: 1097-6744.
CY United States
DT Conference; Conference Article; (CONGRESSES)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200202
ED Entered STN: 20020209
Last Updated on STN: 20020221
Entered Medline: 20020220
CT Check Tags: Human
American Heart Association
Anthranilic Acids: TU, therapeutic use
Antineoplastic Agents: TU, therapeutic use
*Carotid Artery Diseases: TH, therapy
Coronary Disease: DT, drug therapy
*Coronary Disease: PC, prevention & control
Coronary Restenosis
Drug Delivery Systems
Paclitaxel: TU, therapeutic use
Platelet Aggregation Inhibitors: TU, therapeutic use
Platelet Glycoprotein GPIIb-IIIa Complex: AI, antagonists & inhibitors
*Randomized Controlled Trials
***Stents**
RN **33069-62-4 (Paclitaxel)**; 53902-12-8 (Tranilast)
CN 0 (Anthranilic Acids); 0 (Antineoplastic Agents); 0 (Platelet Aggregation Inhibitors); 0 (Platelet Glycoprotein GPIIb-IIIa Complex)

L89 ANSWER 16 OF 17 MEDLINE on STN
AN 2001681488 MEDLINE
DN 21584252 PubMed ID: 11727731
TI American Heart Association 2001 scientific sessions: late-breaking science-drug-eluting **stents**.
AU Fox R
SO CIRCULATION, (2001 Nov 20) 104 (21) E9052.

Journal code: 0147763. ISSN: 1524-4539.
CY United States
DT News Announcement
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200112
ED Entered STN: 20011203
Last Updated on STN: 20020123
Entered Medline: 20011213
CT Check Tags: Human
Clinical Trials
***Coronary Restenosis: DT, drug therapy**
Coronary Restenosis: TH, therapy
Dactinomycin: TU, therapeutic use
Paclitaxel: TU, therapeutic use
Sirolimus: TU, therapeutic use
***Stents**
RN **33069-62-4 (Paclitaxel)**; 50-76-0 (Dactinomycin); 53123-88-9 (Sirolimus)

L89 ANSWER 17 OF 17 MEDLINE on STN
AN 2001467625 MEDLINE
DN 21405304 PubMed ID: 11515015
TI The messenger and the message: Preventing **restenosis.**
CM Comment on: Catheter Cardiovasc Interv. 2001 Aug;53(4):562-8
AU Heldman A W; Brinker J A
SO CATHETERIZATION AND CARDIOVASCULAR INTERVENTIONS, (2001 Aug) 53 (4) 569-70.
Journal code: 100884139. ISSN: 1522-1946.
CY United States
DT Commentary
Editorial
LA English
FS Priority Journals
EM 200110
ED Entered STN: 20010830
Last Updated on STN: 20011015
Entered Medline: 20011011
CT Check Tags: Animal
Angioplasty, Transluminal, Percutaneous Coronary: AE, adverse effects
Antineoplastic Agents, Phytogenic: TU, therapeutic use
Graft Occlusion, Vascular: DT, drug therapy
***Graft Occlusion, Vascular: ET, etiology**
***Graft Occlusion, Vascular: PC, prevention & control**
Hyperplasia: DT, drug therapy
Hyperplasia: ET, etiology
Hyperplasia: PC, prevention & control
Paclitaxel: TU, therapeutic use
Stents: ST, standards
Swine
RN **33069-62-4 (Paclitaxel)**
CN 0 (Antineoplastic Agents, Phytogenic)

=> d l90 all tot

L90 ANSWER 1 OF 55 MEDLINE on STN
AN 2004025449 IN-PROCESS
DN PubMed ID: 14724301
TI A polymer-based, **paclitaxel**-eluting **stent** in patients with coronary artery disease.
AU Stone Gregg W; Ellis Stephen G; Cox David A; Hermiller James;

O'Shaughnessy Charles; Mann James Tift; Turco Mark; Caputo Ronald; Bergin Patrick; Greenberg Joel; Popma Jeffrey J; Russell Mary E
CS Cardiovascular Research Foundation and Lenox Hill Heart and Vascular Institute, New York 10022, USA. (TAXUS-IV Investigators). gstone@crf.org
SO New England journal of medicine, (2004 Jan 15) 350 (3) 221-31.
Journal code: 0255562. ISSN: 1533-4406.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS IN-PROCESS; NONINDEXED; Abridged Index Medicus Journals; Priority Journals
ED Entered STN: 20040116
Last Updated on STN: 20040117
AB BACKGROUND: **Restenosis** after coronary **stenting** necessitates repeated percutaneous or surgical revascularization procedures. The delivery of **paclitaxel** to the site of vascular injury may reduce the incidence of neointimal hyperplasia and **restenosis**. METHODS: At 73 U.S. centers, we enrolled 1314 patients who were receiving a **stent** in a single, previously untreated coronary-artery stenosis (vessel diameter, 2.5 to 3.75 mm; lesion length, 10 to 28 mm) in a prospective, randomized, double-blind study. A total of 652 patients were randomly assigned to receive a bare-metal **stent**, and 662 to receive an identical-appearing, slow-release, polymer-based, **paclitaxel**-eluting **stent**. Angiographic follow-up was prespecified at nine months in 732 patients. RESULTS: In terms of base-line characteristics, the two groups were well matched. Diabetes mellitus was present in 24.2 percent of patients; the mean reference-vessel diameter was 2.75 mm, and the mean lesion length was 13.4 mm. A mean of 1.08 **stents** (length, 21.8 mm) were implanted per patient. The rate of ischemia-driven target-vessel revascularization at nine months was reduced from 12.0 percent with the implantation of a bare-metal **stent** to 4.7 percent with the implantation of a **paclitaxel**-eluting **stent** (relative risk, 0.39; 95 percent confidence interval, 0.26 to 0.59; P<0.001). Target-lesion revascularization was required in 3.0 percent of the group that received a **paclitaxel**-eluting **stent**, as compared with 11.3 percent of the group that received a bare-metal **stent** (relative risk, 0.27; 95 percent confidence interval, 0.16 to 0.43; P<0.001). The rate of angiographic **restenosis** was reduced from 26.6 percent to 7.9 percent with the **paclitaxel**-eluting **stent** (relative risk, 0.30; 95 percent confidence interval, 0.19 to 0.46; P<0.001). The nine-month composite rates of death from cardiac causes or myocardial infarction (4.7 percent and 4.3 percent, respectively) and **stent** thrombosis (0.6 percent and 0.8 percent, respectively) were similar in the group that received a **paclitaxel**-eluting **stent** and the group that received a bare-metal **stent**. CONCLUSIONS: As compared with bare-metal **stents**, the slow-release, polymer-based, **paclitaxel**-eluting **stent** is safe and markedly reduces the rates of clinical and angiographic **restenosis** at nine months.

L90 ANSWER 2 OF 55 MEDLINE on STN
AN 2003559609 IN-PROCESS
DN PubMed ID: 14632945
TI **Paclitaxel**-eluting **stents**: are they all equal? An analysis of six randomized controlled trials in de novo lesions of 3,319 patients.
AU Silber Sigmund
CS Cardiology Practice in the Dr. Muller Hospital, Munich, Germany..
silber@med.de

SO Journal of interventional cardiology, (2003 Dec) 16 (6) 485-90.
Journal code: 8907826. ISSN: 0896-4327.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20031127
Last Updated on STN: 20031219
AB In Germany, four different drug eluting **stents** (DES) systems are currently commercially available. Whereas sirolimus has been clinically tested in only a single type of **stent** with a single type of coating in only a single dose, **paclitaxel** has been tested on various **stent** designs, in various dose densities, and in various release formulations with or without a polymer carrier. Therefore, the question arises: are all **paclitaxel stents** equally safe and effective? Six clinical randomized trials investigated the safety and efficacy of **paclitaxel**-eluting **stents** in patients with de-novo lesions: TAXUS-I (61 pats), TAXUS-II (536 pats), ASPECT (177 pats), ELUTES (190 pats), DELIVER-I (1041 pats) and TAXUS-IV (1314 pats). In the TAXUS-series, **paclitaxel** released from the **stent** was controlled by the Translute polymer. In the other studies, however, no polymer carrier was used. In TAXUS-I, II & IV, the dose density of 1 microg/mm2 significantly reduced angiographic parameters of **restenosis** and improved clinical outcomes. In ASPECT and ELUTES there was a dose-dependent effect on angiographic parameters of **restenosis** with the best results for a **paclitaxel** dose density of approximately 3.0 microg/mm2. Clinical outcomes at 6 and 12 months, however, were not improved in these studies without coating. The studies unanimously show that the **paclitaxel**-eluting **stents** are safe, if clopidogrel is added to ASA for 3 to 6 months. The safety of **paclitaxel**-eluting **stents** is independent of the **stent** design, the dose density and the presence or absence of a polymer carrier system. For **paclitaxel**-eluting **stents** using a polymer carrier, the dose density of 1 microg/mm2 is highly effective, whereas for **paclitaxel**-eluting **stents** without a polymer carrier, the minimal effective dose density is much higher (3 microg/mm2). Despite their improvement of angiographic parameters, **paclitaxel**-eluting **stents** without a polymer carrier did not demonstrate a positive effect on clinical outcome. In contrast, polymer-based **paclitaxel** elution produced significant clinical benefit.

L90 ANSWER 3 OF 55 MEDLINE on STN
AN 2003541499 MEDLINE
DN PubMed ID: 14615021
TI Evolving revascularization approaches for myocardial ischemia.
AU Kleiman Neal S; Patel Nirav C; Allen Keith B; Simons Michael; Yla-Herttuala Seppo; Griffin Elaine; Dzau Victor J
CS Baylor College of Medicine and The Methodist DeBakey Heart Center, Houston, Texas, USA.. nkleiman@bcm.tmc.edu
SO American journal of cardiology, (2003 Nov 7) 92 (9B) 9N-17N. Ref: 80
Journal code: 0207277. ISSN: 0002-9149.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200312
ED Entered STN: 20031119
Last Updated on STN: 20031224
Entered Medline: 20031223
AB Stable angina pectoris secondary to ischemic heart disease is a common and

disabling condition. Medical therapy aims to relieve symptoms, improve exercise capacity, and decrease cardiac events by reducing myocardial oxygen demand or improving coronary blood supply to the ischemic myocardium. If medical treatment is inadequate, invasive revascularization procedures to improve coronary perfusion are considered. Percutaneous transluminal coronary angioplasty (PTCA) and coronary artery bypass graft (CABG) surgery are well-established and widely used myocardial revascularization techniques. Recent advances in PTCA have attempted to address the problem of **restenosis**, initially through the deployment of bare metal intracoronary **stents** and, more recently, with drug-eluting **stents**. Developments in CABG have focused on reducing the invasiveness of the procedure and minimizing the incidence of serious complications. Refinements include the use of mechanical stabilizers, endoscopic harvesting of conduit vessels, robotic telemanipulation systems, and fully automated anastomotic devices. Surgical laser transmyocardial revascularization and therapeutic angiogenesis represent newer approaches to coronary revascularization. Therapeutic angiogenesis aims to deliver an angiogenic growth factor or cytokine to the myocardium to stimulate collateral blood vessel growth throughout the ischemic tissue. The angiogenic factor may be administered as a recombinant protein or as a transgene within a plasmid or gene-transfer vector. Ongoing angiogenic gene therapy clinical trials are evaluating which factors, vectors, and delivery techniques hold the greatest promise for management of patients with chronic stable angina.

CT Check Tags: Human; Support, Non-U.S. Gov't
Angiogenesis Inducing Agents: AD, administration & dosage
Angioplasty, Transluminal, Percutaneous Coronary
Animals
Antineoplastic Agents, Phytogenic: AD, administration & dosage
Coronary Artery Bypass
DNA-Binding Proteins: TU, therapeutic use
Drug Delivery Systems
Fibroblast Growth Factors: AD, administration & dosage
Laser Surgery
*Myocardial Ischemia: SU, surgery
***Myocardial Revascularization: MT, methods**
Nuclear Proteins: TU, therapeutic use
Paclitaxel: AD, administration & dosage
Stents
Vascular Endothelial Growth Factor A: AD, administration & dosage

RN **33069-62-4 (Paclitaxel)**; 62031-54-3 (Fibroblast Growth Factors)

CN 0 (Angiogenesis Inducing Agents); 0 (Antineoplastic Agents, Phytogenic); 0 (DNA-Binding Proteins); 0 (HIF-1 protein); 0 (Nuclear Proteins); 0 (Vascular Endothelial Growth Factor A)

L90 ANSWER 4 OF 55 MEDLINE on STN

AN 2003502025 IN-PROCESS

DN PubMed ID: 14579046

TI Long-term evaluation of **paclitaxel**-coated **stents** for treatment of native coronary lesions. First results of both the clinical and angiographic 18 month follow-up of TAXUS I.

AU Bullesfeld L; Gerckens U; Muller R; Grube E

CS Abt. fur Kardiologie/Angiologie, Krankenhaus and Herzzentrum Siegburg, Ringstrasse 49, 53721 Siegburg, Germany.. LBuellesfeld@gmx.de

SO Zeitschrift fur Kardiologie, (2003 Oct) 92 (10) 825-32.
Journal code: 0360430. ISSN: 0300-5860.

CY Germany: Germany, Federal Republic of

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS IN-PROCESS; NONINDEXED; Priority Journals

ED Entered STN: 20031028
Last Updated on STN: 20031219

AB The development of **restenoses** due to tissue proliferation within

the **stented** segment is a major limitation of conventional **stent** implantations. Recently published studies have shown that drug-eluting **stents** effectively decrease the incidence of **stent restenosis** at 6 month follow-up as compared to bare metal **stents**. However, a persistent efficacy of this **stent** design beyond the 6 month period still needs to be proven. Therefore, in this study, we are demonstrating the first 18 month follow-up results of a **Paclitaxel**-coated coronary **stent**, based on the patient population of the TAXUS I study, a multicenter randomized study to evaluate both safety and efficacy of the **Paclitaxel**-coated NIRx **stent** as compared to an uncoated, bare metal **stent**. In this study we evaluated the long-term outcome of NIRx patients of our center, in which 20 out of 31 patients of the TAXUS I study with NIRx **stent** implantation have been enrolled. A clinical follow-up was available in 20 out of 20 patients (100%) 535 +/- 82 days post **stent** implantation (17.8 months). An angiographic follow-up was available in 14 out of 20 patients (70%) 580 +/- 77 days post **stent** implantation (19.1 months). The MACE rate at 18 month follow-up was 0.0%. There was no **stent restenosis** in the study group up to 18 month post drug-eluting **stent** implantation. There was one non-clinically driven target vessel revascularization due to a **stent** edge lumen renarrowing, which was subsequently calculated as a 43% diameter stenosis. Accordingly, this event was not regarded as MACE. The IVUS analysis of the study population has shown a decrease of the mean minimum lumen area from 8.45 mm(2) postinterventional to 6.87 mm(2) at 6 month follow-up with a relative mean maximum plaque area of 16%. At 18 month follow-up, there were no additional significant changes with a mean minimum lumen area of 7.16 mm(2) and a relative mean maximum plaque area of 13.4%. The reported results of the 18 month follow-up of TAXUS I are the first experiences demonstrating a persistent benefit of the **Paclitaxel**-coated NIRx **stent**. Therefore, this **stent** design seems to be safe and effective, even in long-term follow-up.

L90 ANSWER 5 OF 55 MEDLINE on STN
AN 2003490808 IN-PROCESS
DN PubMed ID: 14568436
TI In vitro hemocompatibility studies of drug-loaded poly-(L-lactic acid) fibers.
AU Nguyen K T; Su S-H; Sheng A; Wawro D; Schwade N D; Brouse C F; Greilich P E; Tang L; Eberhart R C
CS Joint Program in Biomedical Engineering, University of Texas Southwestern Medical Center at Dallas and The University of Texas at Arlington, Dallas, TX 75390, USA.
NC F32 HL010380 (NHLBI)
R01 EB00287 (NIBIB)
R01 HL/DE 53225 (NHLBI)
SO Biomaterials, (2003 Dec) 24 (28) 5191-201.
Journal code: 8100316. ISSN: 0142-9612.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20031022
Last Updated on STN: 20031219
AB Our objective was to evaluate the hemocompatibility of biodegradable **stent** fibers, employing a closed-loop circulation system filled with human blood. We also investigated the effects of the anti-inflammatory and anti-proliferative drugs curcumin and **paclitaxel**, incorporated into **stent** fibers. Fresh whole blood was circulated in four parallel closed-loop systems: the empty tube circuit (control) and tubes containing either a PLLA fiber coil (PLLA), a curcumin-loaded PLLA coil (C-PLLA) or a **paclitaxel**-loaded PLLA

coil (P-PLLA). The influence of PLLA fiber, alone or loaded with drug incorporated during melt-extrusion, on leukocyte and platelet adhesion and activation was determined by flow cytometry. The effects of blood flow and fiber properties on cell deposition were assessed by scanning electron microscopy (SEM). The flow cytometry results clearly demonstrated that PLLA triggers blood cell activation at the site of deployment, as shown by increases in CD11b, CD62P and leukocyte-platelet aggregates, compared to controls. Curcumin and **paclitaxel** treatments both significantly reduced leukocyte and platelet activation and adhesion to PLLA fibers, as shown by flow cytometry and SEM. Activated leukocytes and platelets revealed significantly lower CD11b and CD62P receptor binding for C-PLLA compared with PLLA alone, and slightly lower for P-PLLA. Reductions in platelet-leukocyte aggregates were observed as well. In addition, there was less leukocyte and platelet adhesion to C-PLLA, compared with PLLA fiber controls, as shown by SEM. A continuous linear thrombus, composed of platelets, leukocytes, red blood cells and fibrin was occasionally detected along the line of tangency between the coil and the tube wall. Flow separation and eddying, proximal and distal to the line of tangency of coil and tube, is thought to contribute to this deposit. Curcumin was more effective than **paclitaxel** in reducing leukocyte and platelet activation and adhesion to PLLA **stent** fibers in this setting. However there was evidence of **paclitaxel** degeneration during melt extrusion that may have inhibited its effectiveness. Incorporation of the anti-inflammatory and anti-proliferative drug curcumin into bioresorbable **stent** fibers is proposed to prevent thrombosis and in-**stent restenosis**.

L90 ANSWER 6 OF 55 MEDLINE on STN
AN 2003485617 MEDLINE
DN 22925682 PubMed ID: 14563585
TI Addition of **paclitaxel** to contrast media prevents **restenosis** after coronary **stent** implantation.
AU Scheller Bruno; Speck Ulrich; Schmitt Alexander; Bohm Michael; Nickenig Georg
CS Internal Medicine III (Cardiology/Angiology), University of Saarland, Homburg/Saar, Germany.. bruno.scheller@uniklinik-saarland.de
SO JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY, (2003 Oct 15) 42 (8) 1415-20.
Journal code: 8301365. ISSN: 0735-1097.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200311
ED Entered STN: 20031018
Last Updated on STN: 20031108
Entered Medline: 20031107
AB OBJECTIVES: The present study was designed to test the efficacy of **paclitaxel** added to the contrast agent iopromide in the prevention of **restenosis**. BACKGROUND: Contrast media adhere to the coronary vessel wall for some seconds after injection. Such a layer of contrast agent could serve as a matrix for antiproliferative drugs. METHODS: Thirty-four **stents** were implanted into the left anterior descending and circumflex coronary arteries of 17 pigs, using a 1.2:1.0 overstretch ratio. The unsupplemented contrast agent iopromide-370 was used as a control; the treatment groups were treated with 80 ml intracoronary iopromide plus either 100 or 200 mumol/l **paclitaxel**, or 80 ml intravenous iopromide plus 200 mumol/l **paclitaxel**. Quantitative angiography and histomorphometry were used to assess comparable baseline parameters between the treatment groups. RESULTS: A short time incubation (3 min) almost completely inhibited vascular smooth muscle cell proliferation, sustained for up to 12 days. Whereas intravenous **paclitaxel** had no effect,

intracoronary application of **paclitaxel** reduced the diameter stenosis from 55 +/- 13% to 29 +/- 18% and 13 +/- 12%. Late lumen loss dropped from 1.94 +/- 0.35 mm under the control condition to 1.19 +/- 0.55 mm with 100 mumol/l **paclitaxel** and to 0.82 +/- 0.54 mm with 200 mumol/l **paclitaxel**. Histomorphometry revealed a corresponding dose-dependent reduction of the neointimal area and **restenosis** by intracoronary iopromide **paclitaxel**. Assessment of left ventricular function and myocardial histology revealed no adverse effects of intracoronary **paclitaxel** application. CONCLUSIONS: This study provides evidence that intracoronary application of a taxane dissolved in a contrast medium profoundly inhibits in-**stent restenosis**. This novel, widely feasible approach may be suited for the prevention of **restenosis** in a broad spectrum of interventional treatment regimens.

CT Check Tags: Animal; In Vitro; Support, Non-U.S. Gov't
*Antineoplastic Agents, Phytogenic: AD, administration & dosage
Cells, Cultured
*Contrast Media
***Coronary Restenosis: PC, prevention & control**
Coronary Vessels: DE, drug effects
Iohexol: AD, administration & dosage
*Iohexol: AA, analogs & derivatives
*Iohexol: DU, diagnostic use
***Paclitaxel: AD, administration & dosage**
***Stents**
Swine

RN **33069-62-4 (Paclitaxel)**; 66108-95-0 (Iohexol); 73334-07-3 (iopromide)

CN 0 (Antineoplastic Agents, Phytogenic); 0 (Contrast Media)

L90 ANSWER 7 OF 55 MEDLINE on STN
AN 2003485053 MEDLINE
DN 22925067 PubMed ID: 14564301
TI Drug-eluting **stents** and glycoprotein IIb/IIIa inhibitors: combination therapy for the future.
AU Leon Martin B; Bakhai Ameet
CS Cardiovascular Research Foundation, Lennox Hill Hospital, New York, NY 10012, USA.. MLeon@LenoxHill.Net
SO AMERICAN HEART JOURNAL, (2003 Oct) 146 (4 Suppl) S13-7. Ref: 28
Journal code: 0370465. ISSN: 1097-6744.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200310
ED Entered STN: 20031018
Last Updated on STN: 20031024
Entered Medline: 20031023

AB BACKGROUND: Although coronary **stenting** has improved the results of coronary interventions compared to coronary angioplasty alone, in-**stent restenosis** remains a significant limitation of this procedure. Drug-eluting **stents** with or without glycoprotein IIb/IIIa inhibitor therapy represent an additional advance in the evolution of this strategy. METHODS: We review the currently available trials comparing studies of non-drug-eluting and drug-eluting **stents** using sirolimus and **paclitaxel** agents and their derivatives. RESULTS: Ten studies are available that compare drug-eluting to traditional non-drug-eluting **stents**. A variety of antiplatelet regimes have been used. The majority of these studies are in the process of being published. No head-to-head studies comparing different drug-eluting **stents** are available. CONCLUSIONS:

Drug-eluting **stents** using sirolimus and **paclitaxel** in combination with enhanced antiplatelet strategies represent an important advantage over non-drug-eluting **stents** for the reduction of in-**stent restenosis**. The rate at which drug-eluting **stents** are adapted into widespread practice depends heavily on whether they are safe, efficacious, and cost-effective in various clinical settings.

CT Check Tags: Human
Angioplasty, Transluminal, Percutaneous Coronary
*Antineoplastic Agents: TU, therapeutic use
Clinical Trials
Combined Modality Therapy
Coronary Restenosis: ET, etiology
***Coronary Restenosis: PC, prevention & control**
Diabetic Angiopathies: ET, etiology
Diabetic Angiopathies: PC, prevention & control
***Paclitaxel: TU, therapeutic use**
*Platelet Glycoprotein GPIIb-IIIa Complex: AI, antagonists & inhibitors
*Sirolimus: TU, therapeutic use
***Stents**
Stents: AE, adverse effects

RN **33069-62-4 (Paclitaxel)**; 53123-88-9 (Sirolimus)
CN 0 (Antineoplastic Agents); 0 (Platelet Glycoprotein GPIIb-IIIa Complex)

L90 ANSWER 8 OF 55 MEDLINE on STN
AN 2003433999 MEDLINE
DN 22855428 PubMed ID: 12952833
TI Impact of preinterventional arterial remodeling on neointimal hyperplasia after implantation of (non-polymer-encapsulated) **paclitaxel**-coated **stents**: a serial volumetric intravascular ultrasound analysis from the ASian **Paclitaxel**-Eluting **Stent** Clinical Trial (ASPECT).
AU Mintz Gary S; Tinana Adrienne; Hong Myeong-Ki; Lee Cheol Whan; Kim Jae-Joong; Fearnot Neal E; Park Seong-Wook; Park Seung-Jung; Weissman Neil J
CS Cardiovascular Research Foundation, New York, NY, USA.
SO CIRCULATION, (2003 Sep 16) 108 (11) 1295-8.
Journal code: 0147763. ISSN: 1524-4539.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200309
ED Entered STN: 20030917
Last Updated on STN: 20031001
Entered Medline: 20030930
AB BACKGROUND: This study used serial volumetric intravascular ultrasound (IVUS) to evaluate the effect of preinterventional arterial remodeling on in-**stent** intimal hyperplasia (IH) after implantation of non-polymer-encapsulated **paclitaxel**-coated **stents**.
METHODS AND RESULTS: Patients were randomized to placebo or one of two doses of **paclitaxel** (low dose, 1.28 microg/mm2; high dose, 3.10 microg/mm2). Complete preinterventional, post-**stent** implantation, and follow-up IVUS were available in 18 low-dose and 21 high-dose patients. IH volumes were similar in low-dose and high-dose patients: 17.6+/-15.1 mm3 in low-dose patients and 13.1+/-13.3 mm3 in high-dose patients (P=0.3). Therefore, IVUS findings in low- and high-dose patients were combined. Preinterventional remodeling was assessed by comparing lesion site to proximal and distal reference arterial area: positive remodeling (lesion>proximal reference, n=13),

intermediate remodeling (distal reference<lesion<proximal reference, n=13), and negative remodeling (lesion<distal reference, n=13). During follow-up, there was a decrease in lumen volume in positive remodeling lesions (from 106+/-30 to 90+/-27 mm3; P=0.0067) and in intermediate remodeling lesions (from 97+/-28 to 76+/-31 mm3; P=0.0004), but not in negative remodeling lesions (99+/-27 versus 92+/-32 mm3; P=0.15). The follow-up IH volume was lower in negative remodeling lesions (5+/-7 mm3) compared with positive remodeling (20+/-14 mm3; P=0.0051) and intermediate remodeling lesions (20+/-15 mm3; P=0.0043); however, IH volume was virtually identical in positive and intermediate remodeling lesions. Multivariate linear regression analysis determined that remodeling and inflation pressure were independent predictors of IH volume; variables tested in the model included diabetes, acute coronary syndromes, dose, remodeling, and preinterventional plaque burden. CONCLUSIONS: Preinterventional arterial remodeling, especially negative remodeling, influences neointimal hyperplasia suppression after implantation of non-polymer-encapsulated **paclitaxel**-coated **stents**.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
Coronary Restenosis: ET, etiology
Coronary Restenosis: PA, pathology
***Coronary Restenosis: PC, prevention & control**
Coronary Restenosis: US, ultrasonography
Hyperplasia
Middle Age
Paclitaxel: AD, administration & dosage
***Paclitaxel: TU, therapeutic use**
***Stents**
Stents: AE, adverse effects
Tunica Intima: PA, pathology
Tunica Intima: US, ultrasonography

RN **33069-62-4 (Paclitaxel)**

L90 ANSWER 9 OF 55 MEDLINE on STN
AN 2003426593 MEDLINE
DN PubMed ID: 12966638
TI [Drug releasing **stents**].
Stents liberadores de farmacos.
AU Ban Hayashi Ernesto
CS Departamento de Hemodinamica, Instituto Nacional de Cardiologia Ignacio Chavez INCICH, Juan Badiano No. 1, Col. Seccion, XVI, Tlalpan, 14080 Mexico D.F.
SO Archivos de cardiologia de Mexico, (2003 Apr-Jun) 73 Suppl 1 S17-20. Journal code: 101126728. ISSN: 1405-9940.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA Spanish
FS Priority Journals
EM 200312
ED Entered STN: 20030912
Last Updated on STN: 20031224
Entered Medline: 20031223
AB Drug eluting **stents** have become a mainstream in the treatment of coronary heart disease. Implementation of this technology into medical practice has resulted in a dramatic reduction in **restenosis** rates and late loss, which in turn is reflected in a significant reduction in MACE events due predominantly to a reduction in the need of a new re-intervention in the treated vessel. Historical comparisons between surgical results and the recently published studies with drug eluting **stents** shows that survival free of major events and the need of new revascularization are about the same in both groups of patients.
CT Check Tags: Human
Antibiotics, Antineoplastic: AD, administration & dosage
Antineoplastic Agents, Phytogenic: AD, administration & dosage

Clinical Trials
*Coronary Disease: DT, drug therapy
*Drug Delivery Systems
English Abstract
Muscle, Smooth, Vascular: DE, drug effects
Paclitaxel: AD, administration & dosage
Sirolimus: AD, administration & dosage
***Stents**
RN **33069-62-4 (Paclitaxel)**; 53123-88-9 (Sirolimus)
CN 0 (Antibiotics, Antineoplastic); 0 (Antineoplastic Agents, Phytogenic)

L90 ANSWER 10 OF 55 MEDLINE on STN
AN 2003404088 MEDLINE
DN 22791235 PubMed ID: 12909076
TI Contrast media as carriers for local drug delivery. Successful inhibition of neointimal proliferation in the porcine coronary **stent** model.
AU Scheller Bruno; Speck Ulrich; Romeike Bernd; Schmitt Alexander; Sovak Milos; Bohm Michael; Stoll Hans Peter
CS Internal Medicine III, University of Saarland, D-66421 Homburg/Saar, Germany.. bruno.scheller@uniklinik-saarland.de
SO EUROPEAN HEART JOURNAL, (2003 Aug) 24 (15) 1462-7.
Journal code: 8006263. ISSN: 0195-668X.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200310
ED Entered STN: 20030829
Last Updated on STN: 20031008
Entered Medline: 20031006
AB BACKGROUND: Lipophilic taxanes can be dissolved in contrast media at significantly higher concentration than in saline. As contrast media have occasionally been observed to delineate the contour of coronary arteries for some seconds they may serve as a matrix for an antiproliferative drug aimed at preventing **restenosis**. The aim of this study was to test a novel taxane-contrast agent formulation for this new approach in the setting of coronary **stenting**. METHODS AND RESULTS: In cell culture experiments (bovine vascular smooth muscle cells), 60-min incubation with contrast agent-taxane formulations (iopromide-**paclitaxel**, iopromide-protaxel) induced a significant, concentration-dependent inhibition of vascular smooth muscle cell (VSMC) proliferation over 12 days. Shorter incubation times of 10 and 3 min showed the same efficacy. For in vivo investigation, 16 **stents** were implanted into the coronary arteries of eight pigs using a 1.3 to 1 overstretch ratio. A control group received iopromide 370 alone while the treatment group was injected with a iopromide-protaxel formulation at a dose of 74 micromol/l, which is far below protaxel levels inducing systemic toxicity. Quantitative angiography and histomorphometry of the **stented** arteries asserted statistic equality of the baseline parameters between the control and treatment groups. After 28 days, the treatment group showed a marked reduction of the parameters characterizing in-**stent restenosis**, especially a 34% reduction of the neointimal area. CONCLUSIONS: First evidence is provided that using a contrast agent as solvent for a taxane constitutes a new drug delivery mechanism able to inhibit in-**stent restenosis** in the porcine **restenosis** model.
CT Check Tags: Animal; Support, Non-U.S. Gov't
Cell Division: DE, drug effects
*Contrast Media: AD, administration & dosage
Coronary Restenosis: PA, pathology
Coronary Restenosis: PC, prevention & control
Drug Carriers
Feasibility Studies

*Iohexol: AD, administration & dosage
*Iohexol: AA, analogs & derivatives
***Paclitaxel: AD, administration & dosage**
***Paclitaxel: AA, analogs & derivatives**
***Stents**
Swine
Tunica Intima: PA, pathology
RN **33069-62-4 (Paclitaxel)**; 66108-95-0 (Iohexol); 73334-07-3 (iopromide)
CN 0 (Contrast Media); 0 (Drug Carriers); 0 (protaxel)

L90 ANSWER 11 OF 55 MEDLINE on STN
AN 2003400522 MEDLINE
DN 22820034 PubMed ID: 12938576
TI [In-**stent restenosis**: which indications for drug-eluting **stent**?].
La **restenose** intrastent: quelles indications pour le **stent** actif?.
AU Eltchaninoff H; Tron C; Cribier A
CS Service de cardiologie, hopital Charles-Nicolle, 1, rue de Germont, 76031 Rouen, France.. helene.eltchaninoff@chu-rouen.fr
SO ANNALES DE CARDIOLOGIE ET D ANGEIOLOGIE, (2003 Jun) 52 (3) 198-9. Journal code: 0142167. ISSN: 0003-3928.
CY France
DT Journal; Article; (JOURNAL ARTICLE)
LA French
FS Priority Journals
EM 200311
ED Entered STN: 20030827
Last Updated on STN: 20031113
Entered Medline: 20031112
AB In-**stent restenosis** remains a limitation of **stent** implantation. Currently, at the exception of brachytherapy, any percutaneous technique is associated with a high recurrent **restenosis** rate (> 50%) in diffuse in-**stent restenosis**. Although based on a small number of patients, eluting **stents** (sirolimus, **paclitaxel**) appear promising for the treatment of instent **restenosis**.
CT Check Tags: Comparative Study; Human
*Angiogenesis Inhibitors: AD, administration & dosage
***Angioplasty, Transluminal, Percutaneous Coronary**
*Antibiotics, Macrolide: AD, administration & dosage
Clinical Trials
Coated Materials, Biocompatible
Coronary Angiography
Coronary Restenosis: CO, complications
Coronary Restenosis: DI, diagnosis
***Coronary Restenosis: PC, prevention & control**
Coronary Restenosis: RA, radiography
*Drug Delivery Systems
Echocardiography
English Abstract
Follow-Up Studies
*Immunosuppressive Agents: AD, administration & dosage
Middle Age
***Paclitaxel: AD, administration & dosage**
Risk Factors
*Sirolimus: AD, administration & dosage
***Stents**
Time Factors
RN **33069-62-4 (Paclitaxel)**; 53123-88-9 (Sirolimus)
CN 0 (Angiogenesis Inhibitors); 0 (Antibiotics, Macrolide); 0 (Coated Materials, Biocompatible); 0 (Immunosuppressive Agents)

L90 ANSWER 12 OF 55 MEDLINE on STN
AN 2003388285 MEDLINE
DN 22806325 PubMed ID: 12900339
TI Randomized study to assess the effectiveness of slow- and moderate-release polymer-based **paclitaxel**-eluting **stents** for coronary artery lesions.
AU Colombo Antonio; Drzewiecki Janusz; Banning Adrian; Grube Eberhard; Hauptmann Karl; Silber Sigmund; Dudek Dariusz; Fort Stephen; Schiele Francois; Zmudka Krysztof; Guagliumi Giulio; Russell Mary E
CS Ospedale San Raffaele, Milano, Italy. (TAXUS II Study Group). colombo@emocolumbus.it
SO CIRCULATION, (2003 Aug 19) 108 (7) 788-94.
Journal code: 0147763. ISSN: 1524-4539.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200309
ED Entered STN: 20030820
Last Updated on STN: 20030923
Entered Medline: 20030922
AB BACKGROUND: Early clinical studies demonstrated the feasibility of local **paclitaxel** delivery in reducing **restenosis** after treatment of de novo coronary lesions in small patient populations. METHODS AND RESULTS: We conducted a randomized, double-blind trial of 536 patients at 38 medical centers evaluating slow-release (SR) and moderate-release (MR) formulations of a polymer-based **paclitaxel** -eluting **stent** (TAXUS) for revascularization of single, primary lesions in native coronary arteries. Cohort I compared TAXUS-SR with control **stents**, and Cohort II compared TAXUS-MR with a second control group. The primary end point was 6-month percent in-**stent** net volume obstruction measured by intravascular ultrasound. Secondary end points were 6-month angiographic **restenosis** and 6- and 12-month incidence of major adverse cardiac events, a composite of cardiac death, myocardial infarction, and repeat revascularization. At 6 months, percent net volume obstruction within the **stent** was significantly lower for TAXUS **stents** (7.9% SR and 7.8% MR) than for respective controls (23.2% and 20.5%; P<0.0001 for both). This corresponded with a reduction in angiographic **restenosis** from 17.9% to 2.3% in the SR cohort (P<0.0001) and from 20.2% to 4.7% in the MR cohort (P=0.0002). The incidence of major adverse cardiac events at 12 months was significantly lower (P=0.0192) in the TAXUS-SR (10.9%) and TAXUS-MR (9.9%) groups than in controls (22.0% and 21.4%, respectively), predominantly because of a significant reduction in repeat revascularization of the target lesion in TAXUS-treated patients. CONCLUSIONS: Compared with a bare metal **stent**, **paclitaxel**-eluting **stents** reduced in-**stent** neointimal formation and **restenosis** and improved 12-month clinical outcome of patients with single de novo coronary lesions.
CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
*Coated Materials, Biocompatible: AD, administration & dosage
Cohort Studies
Coronary Angiography
*Coronary Arteriosclerosis: SU, surgery
*Delayed-Action Preparations: AD, administration & dosage
Delayed-Action Preparations: AE, adverse effects
Disease-Free Survival
*Drug Implants: AD, administration & dosage
Drug Implants: AE, adverse effects

Follow-Up Studies
Hemorrhage: ET, etiology
Middle Age
Postoperative Complications: ET, etiology
*Stents
Stents: AE, adverse effects
Stents: ST, standards
Thrombosis: ET, etiology
Treatment Outcome
Ultrasonography, Interventional
CN 0 (Coated Materials, Biocompatible); 0 (Delayed-Action Preparations); 0 (Drug Implants)

L90 ANSWER 13 OF 55 MEDLINE on STN
AN 2003267960 IN-PROCESS
DN PubMed ID: 12793972
TI Drug-eluting **Stents** for Cardiovascular Disorders.
AU Granada Juan F; Kaluza Grzegorz L; Raizner Albert
CS The Methodist DeBakey Heart Center, Baylor College of Medicine, 6535 Fannin, Room FB 1034, Houston, TX 77030, USA.. araizner@tmh.tmc.edu
SO Current atherosclerosis reports, (2003 Jul) 5 (4) 308-16.
Journal code: 100897685. ISSN: 1523-3804.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-DATA-REVIEW; IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20030610
Last Updated on STN: 20031218
AB Drug-eluting **stents** have emerged in recent years as a very promising therapy for prevention of **restenosis** after coronary implantation. Early randomized, clinical trials have suggested that **stents** eluting drugs, such as **paclitaxel** or sirolimus, released from polymeric and nonpolymeric coatings, are able to reduce **restenosis** in simple de novo lesions by more than 80% in comparison with bare metal **stents**. If **restenosis** can be indeed minimized globally by drug-eluting **stents**, coronary revascularization may expand to patients and lesions currently not considered for percutaneous intervention because of excessive recurrence, and may open possibilities for other **stent**-based endovascular treatments of atherosclerosis.

L90 ANSWER 14 OF 55 MEDLINE on STN
AN 2003259860 IN-PROCESS
DN PubMed ID: 12784776
TI Through the drug-eluting **stent** labyrinth.
AU Guagliumi Giulio; Musumeci Giuseppe; Vassileva Angelina; Tespili Maurizio; Valsecchi Orazio
CS Cardiovascular Department, Ospedali Riuniti, Bergamo.. guagliumig@interfree.it
SO Italian heart journal : official journal of the Italian Federation of Cardiology, (2003 Apr) 4 (4) 236-45.
Journal code: 100909716. ISSN: 1129-471X.
CY Italy
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20030606
Last Updated on STN: 20031217
AB For interventional cardiologists **restenosis** has represented the main limit for the successful long-term treatment of coronary artery disease. The past 2 years witnessed the extraordinary results of drug-eluting **stents** (DES), putting this technique at the center stage. The safety and efficacy of sirolimus and **paclitaxel**

-eluting **stents** have been proved in large prospective, multicenter, randomized trials (RAVEL, SIRIUS, TAXUS II). It is possible that the introduction of DES will lead to substantial changes in the therapeutic and/or the economic strategies of the treatment of ischemic coronary artery disease (increase in the complexity of patients treated, reduction in surgical indications, growing costs). Realizing the potential value of this technology will require the successful management of more complex coronary situations (for lesions and patients characteristics). Many extreme situations are still unexplored, although for some of them studies are currently in progress or already being planned.

L90 ANSWER 15 OF 55 MEDLINE on STN
AN 2003211946 MEDLINE
DN 22618589 PubMed ID: 12732447
TI Molecular mechanisms of **in-stent restenosis** and approach to therapy with eluting **stents**.
AU Indolfi Ciro; Mongiardo Annalisa; Curcio Antonio; Torella Daniele
CS Division of Cardiology, Magna Graecia University, Catanzaro, Italy.. indolfi@unicz.it
SO TRENDS IN CARDIOVASCULAR MEDICINE, (2003 May) 13 (4) 142-8. Ref: 43
Journal code: 9108337. ISSN: 1050-1738.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200309
ED Entered STN: 20030507
Last Updated on STN: 20030905
Entered Medline: 20030904
AB **Restenosis** is the principal drawback of percutaneous coronary procedures. Until now, the only widely accepted way to reduce **restenosis** rate has been the **stent**. However, clinical **restenosis** still represents the major limitation of this technology. This article summarizes recent laboratory and clinical investigations concerning the mechanisms responsible for the transmission of mitogenic signals from plasma membrane to the nucleus in vascular smooth muscle cells that determine neointima formation after **stent** deployment. Recent experimental data on the impact of diabetes and physical exercise on **restenosis** also is reviewed. Finally, the new concept of local drugs that elute directly to the site of vascular injury from coated **stents** and the available clinical results obtained with rapamycin or **paclitaxel**-eluting **stents** are discussed.
CT Check Tags: Animal; Human
Angioplasty, Transluminal, Percutaneous Coronary
Blood Vessel Prosthesis Implantation
*Coated Materials, Biocompatible: TU, therapeutic use
***Coronary Restenosis: ET, etiology**
Coronary Restenosis: PP, physiopathology
***Coronary Restenosis: TH, therapy**
Muscle, Smooth, Vascular: CY, cytology
Muscle, Smooth, Vascular: PP, physiopathology
Signal Transduction: PH, physiology
***Stents**
CN 0 (Coated Materials, Biocompatible)

L90 ANSWER 16 OF 55 MEDLINE on STN
AN 2003210846 MEDLINE
DN 22617282 PubMed ID: 12731426
TI [Coronary **stents**].

Koronare **Stents.**
AU Amann F W
CS Herz-Gefasszentrum Zurich, Klinik im Park, Zurich..
franz.amann@hirslanden.ch
SO THERAPEUTISCHE UMSCHAU, (2003 Apr) 60 (4) 179-82.
Journal code: 0407224. ISSN: 0040-5930.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA German
FS Priority Journals
EM 200306
ED Entered STN: 20030507
Last Updated on STN: 20030627
Entered Medline: 20030626
AB Since the introduction of coronary **stents** into clinical practice in the late 1980s, the number of **stent** implantations has increased so rapidly that **stents** are currently used in over 80 percent of all percutaneous coronary interventions. Although **stent** implantation was initially limited to large vessels with proximal and discrete lesions, improvements in **stent** design and implantation technique now allow their deployment in more complex lesions in smaller and diffusely diseased vessels. The overall acceptance of **stents** by interventional cardiologists can be attributed to favorable acute and longterm results compared to balloon angioplasty alone. Interventionalists have also been quick to embrace the smoother and larger lumen after **stenting**, in a shorter procedure time and with no additional risk, especially since the risk of **stent** thrombosis has been overcome by the introduction of dual antiplatelet therapy with Aspirin and Ticlopidine or Clopidogrel. Although **restenosis** and the need for reinterventions is lower after **stenting** compared to balloon angioplasty it still remains significant with about 15 percent of all patients returning for an other revascularization procedure. Meanwhile, a completely new generation of **stents** promises to eliminate the problem of **restenosis**. Drug-eluting **stents**, coated with antiproliferative substances have been successfully tested in small randomized trials. The **restenosis** rates at 6 and 12 months were extremely low ranging between zero and nine percent, with no clinical drawbacks so far. If these results hold up in longer follow up and in real life practice with more complex lesions **stented** the treatment of symptomatic coronary artery disease will change even more dramatically.
CT Check Tags: Human
Angiogenesis Inhibitors: AD, administration & dosage
Angiogenesis Inhibitors: TU, therapeutic use
***Angioplasty, Transluminal, Percutaneous Coronary**
Controlled Clinical Trials
*Coronary Disease: TH, therapy
Coronary Restenosis: PC, prevention & control
Double-Blind Method
English Abstract
Follow-Up Studies
Paclitaxel: AD, administration & dosage
Paclitaxel: TU, therapeutic use
Prosthesis Design
Reoperation
Risk Factors
Sirolimus: TU, therapeutic use
***Stents**
Stents: AE, adverse effects
Time Factors
RN **33069-62-4 (Paclitaxel)**; 53123-88-9 (Sirolimus)
CN 0 (Angiogenesis Inhibitors)

L90 ANSWER 17 OF 55 MEDLINE on STN
AN 2003181925 MEDLINE
DN 22586802 PubMed ID: 12700373
TI A **paclitaxel**-eluting **stent** for the prevention of coronary **restenosis**.
CM Comment in: N Engl J Med. 2003 May 29;348(22):2254
AU Park Seung-Jung; Shim Won Heum; Ho David S; Raizner Albert E; Park Seong-Wook; Hong Myeong-Ki; Lee Cheol Whan; Choi Donghoon; Jang Yangsoo; Lam Ricky; Weissman Neil J; Mintz Gary S
CS Asan Medical Center, Seoul, South Korea.. sjpark@amc.seoul.kr
SO NEW ENGLAND JOURNAL OF MEDICINE, (2003 Apr 17) 348 (16) 1537-45. Journal code: 0255562. ISSN: 1533-4406.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200304
ED Entered STN: 20030418
Last Updated on STN: 20030424
Entered Medline: 20030423
AB BACKGROUND: Intimal hyperplasia and resulting **restenosis** limit the efficacy of coronary **stenting**. We studied a coronary **stent** coated with the antiproliferative agent **paclitaxel** as a means of preventing **restenosis**. METHODS: We conducted a multicenter, randomized, controlled, triple-blind study to evaluate the ability of a **paclitaxel**-eluting **stent** to inhibit **restenosis**. At three centers, 177 patients with discrete coronary lesions (<15 mm in length, 2.25 to 3.5 mm in diameter) underwent implantation of **paclitaxel**-eluting **stents** (low dose, 1.3 microg per square millimeter, or high dose, 3.1 microg per square millimeter) or control **stents**. Antiplatelet therapies included aspirin with ticlopidine (120 patients), clopidogrel (18 patients), or cilostazol (37 patients). Clinical follow-up was performed at one month and four to six months, and angiographic follow-up at four to six months. RESULTS: Technical success was achieved in 99 percent of the patients (176 of 177). At follow-up, the high-dose group, as compared with the control group, had significantly better results for the degree of stenosis (mean [+/-SD], 14+/-21 percent vs. 39+/-27 percent; P<0.001), late loss of luminal diameter (0.29+/-0.72 mm vs. 1.04+/-0.83 mm, P<0.001), and **restenosis** of more than 50 percent (4 percent vs. 27 percent, P<0.001). Intravascular ultrasound analysis demonstrated a dose-dependent reduction in the volume of intimal hyperplasia (31, 18, and 13 mm3, in the high-dose, low-dose, and control groups, respectively). There was a higher rate of major cardiac events in patients receiving cilostazol than in those receiving ticlopidine or clopidogrel. Among patients receiving ticlopidine or clopidogrel, event-free survival was 98 percent and 100 percent in the high-dose and control groups, respectively, at one month, and 96 percent in both at four to six months. CONCLUSIONS: **Paclitaxel**-eluting **stents** used with conventional antiplatelet therapy effectively inhibit **restenosis** and neointimal hyperplasia, with a safety profile similar to that of standard **stents**.

CT Check Tags: Comparative Study; Female; Human; Male; Support, Non-U.S. Gov't
Angiogenesis Inhibitors: AD, administration & dosage
Angiogenesis Inhibitors: AE, adverse effects
*Angiogenesis Inhibitors: TU, therapeutic use
Angioplasty, Transluminal, Percutaneous Coronary
Aspirin: AE, adverse effects

Aspirin: TU, therapeutic use
Coronary Angiography
Coronary Disease: PA, pathology
Coronary Disease: RA, radiography
*Coronary Disease: TH, therapy
***Coronary Restenosis: PC, prevention & control**
Coronary Restenosis: RA, radiography
Coronary Restenosis: US, ultrasonography
Dose-Response Relationship, Drug
Double-Blind Method
Drug Therapy, Combination
Hyperplasia: PC, prevention & control
Hyperplasia: US, ultrasonography
Middle Age
Paclitaxel: AD, administration & dosage
Paclitaxel: AE, adverse effects
***Paclitaxel: TU, therapeutic use**
Platelet Aggregation Inhibitors: AE, adverse effects
Platelet Aggregation Inhibitors: TU, therapeutic use
***Stents**
Ticlopidine: AE, adverse effects
Ticlopidine: AA, analogs & derivatives
Ticlopidine: TU, therapeutic use
Tunica Intima: PA, pathology
Ultrasonography, Interventional
RN **33069-62-4 (Paclitaxel)**; 50-78-2 (Aspirin); 55142-85-3 (Ticlopidine); 90055-48-4 (clopidogrel)
CN 0 (Angiogenesis Inhibitors); 0 (Platelet Aggregation Inhibitors)

L90 ANSWER 18 OF 55 MEDLINE on STN
AN 2003127376 MEDLINE
DN 22528263 PubMed ID: 12641014
TI Drug eluting **stents**: initial experiences.
AU Grube E; Gerckens U; Muller R; Bullesfeld L
CS Heart-Center Siegburg Ringstrasse 49 53721 Siegburg, Germany..
GrubeE@aol.com
SO ZEITSCHRIFT FUR KARDIOLOGIE, (2002) 91 Suppl 3 44-8.
Journal code: 0360430. ISSN: 0300-5860.
CY Germany: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200303
ED Entered STN: 20030319
Last Updated on STN: 20030331
Entered Medline: 20030328
AB Local delivery of immunosuppressive or antiproliferative agents using a drug-eluting **stent** is a new technology meant to inhibit in-**stent restenosis** providing both a biological and mechanical solution and has recently emerged as a very promising approach. Up to now several agents have been in use: **Paclitaxel**, Rapamycin, Actinomycin D or Tacrolimus. Evaluating these drugs regarding their release kinetics, effective dosage, safety in clinical practice and benefit, several studies have been published or are still ongoing: SCORE (**Paclitaxel**-derivative), TAXUS I, II, III, IV (**Paclitaxel**), ELUTE, ASPECT (**Paclitaxel**), RAVEL, SIRIUS (Sirolimus), ACTION (Actinomycin), EVIDENT, PRESENT (Tacrolimus). **Paclitaxel** was the first **stent**-based antiproliferative agent under clinical investigation providing profound inhibition of neointimal thickening, depending on delivery duration and drug dosage. The randomized multicenter SCORE trail (Quanam **stent**, **Paclitaxel** coated) enrolled 266 patients at 17 sites. At 6 month follow-up, a drop of 83% in **stent restenosis** using the drug-eluting

stent could be achieved (6.4% drug-eluting **stent** vs. 36.9% control group) attributable to a remarkable decrease in intimal proliferation. Unfortunately, due to both frequent **stent** thrombosis and side-branch occlusions the reported 30-day MACE rate was 10.2%. The randomized TAXUS I safety trail (NIRx, **Paclitaxel** coated) also demonstrated beneficial reduction of restenotic lesions at 6-month FU (0% vs. 11%) but, this time, associated with the absence of thrombotic events presumably due to the lower drug dosage. The ongoing TAXUS II, III and IV trails are aimed at providing additional insight regarding the efficacy of the TAXUS **Paclitaxel**-eluting **stent**. Both the RAVEL and the SIRIUS trial have been conducted to evaluate a Sirolimus-coated **stent** (Bx VELOCITY **stent**). From the results available, the beneficial findings regarding reduction of renarrowing using a drug-eluting **stent** have been confirmed without any adverse effects. Although parameters like drug toxicity, optimal drug dosage or delayed endothelial healing need to be further evaluated, summarizing the today's clinical experience the strategy of drug-coated **stents** promises a striking benefit in interventional treatment of coronary lesions.

CT Check Tags: Animal; Comparative Study; Human
*Angiogenesis Inhibitors: AD, administration & dosage
***Angioplasty, Transluminal, Percutaneous Coronary**
Coated Materials, Biocompatible
***Coronary Restenosis: PC, prevention & control**
Dactinomycin: AD, administration & dosage
*Drug Delivery Systems
Follow-Up Studies
*Immunosuppressive Agents: AD, administration & dosage
Multicenter Studies
Paclitaxel: AD, administration & dosage
Pilot Projects
Protein Synthesis Inhibitors: AD, administration & dosage
Randomized Controlled Trials
Safety
Sirolimus: AD, administration & dosage
***Stents**
Stents: AE, adverse effects
Swine
Tacrolimus: AD, administration & dosage
Time Factors

RN 109581-93-3 (Tacrolimus); **33069-62-4 (Paclitaxel)**; 50-76-0 (Dactinomycin); 53123-88-9 (Sirolimus)

CN 0 (Angiogenesis Inhibitors); 0 (Coated Materials, Biocompatible); 0 (Immunosuppressive Agents); 0 (Protein Synthesis Inhibitors)

L90 ANSWER 19 OF 55 MEDLINE on STN
AN 2003118528 MEDLINE
DN 22519263 PubMed ID: 12631633
TI Drug-eluting **stents**: potential applications for peripheral arterial occlusive disease.
AU Duda Stephan H; Poerner Tudor C; Wiesinger Benjamin; Rundback John H; Tepe Gunnar; Wiskirchen Jakub; Haase Karl K
CS Department of Diagnostic Radiology, University of Tuebingen, Germany.. stephan.duda@med.uni-tuebingen.de
SO JOURNAL OF VASCULAR AND INTERVENTIONAL RADIOLOGY, (2003 Mar) 14 (3) 291-301. Ref: 87
Journal code: 9203369. ISSN: 1051-0443.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
LA English
FS Priority Journals

EM 200306
ED Entered STN: 20030313
Last Updated on STN: 20030614
Entered Medline: 20030613
AB Many different approaches have been evaluated to prevent **restenosis** in **stents** after vascular implantation. Currently, drug-eluting **stents** are extremely promising in suppressing neointimal hyperplasia. Various animal studies and randomized trials in humans have shown excellent results in terms of safety and efficacy during intermediate-term follow-up. This article will give an overview of experimental and clinical data of the different agents in published and ongoing trials.
CT Check Tags: Human
Angiogenesis Inhibitors: AD, administration & dosage
Anti-Inflammatory Agents, Steroidal: AD, administration & dosage
*Arterial Occlusive Diseases: PC, prevention & control
***Coronary Restenosis: PC, prevention & control**
Dexamethasone: AD, administration & dosage
Drug Delivery Systems
Immunosuppressive Agents: AD, administration & dosage
Paclitaxel: AD, administration & dosage
Prosthesis Design
Recurrence
Sirolimus: AD, administration & dosage
***Stents**
***Vascular Patency**
RN **33069-62-4 (Paclitaxel)**; 50-02-2 (Dexamethasone); 53123-88-9 (Sirolimus)
CN 0 (Angiogenesis Inhibitors); 0 (Anti-Inflammatory Agents, Steroidal); 0 (Immunosuppressive Agents)

L90 ANSWER 20 OF 55 MEDLINE on STN
AN 2003101680 MEDLINE
DN 22501370 PubMed ID: 12613364
TI [The best of coronary atheroma and interventional cardiology in 2002]. L'essentiel de 2002 en atherome coronaire et cardiologie interventionnelle.
AU Chevalier B
CS Centre cardiologique du Nord, service d'hemodynamique, 32-36, avenue des-Moulins Gemeaux, 93207 Saint-Denis.
SO ARCHIVES DES MALADIES DU COEUR ET DES VAISSEAUX, (2003 Jan) 96 Spec No 1 57-60. Ref: 23
Journal code: 0406011. ISSN: 0003-9683.
CY France
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA French
FS Priority Journals
EM 200304
ED Entered STN: 20030305
Last Updated on STN: 20030408
Entered Medline: 20030407
AB The year 2002 in interventional cardiology was monopolised by the concept of the active **stent**. Each step of the **restenosis** process can be targeted by the active principle: platelet thrombosis, inflammation, smooth muscle cell migration, smooth muscle cell proliferation. At this stage, only sirolimus and **paclitaxel** have successfully completed the clinical validation process in simple lesions. Certain questions remain unresolved: far from 0% **restenosis**, why are these devices less effective in lesions at high risk of **restenosis**? Why does sirolimus **stent** usage create effects of **restenosis** on the edges and why is it

present in cases of positive remodelling of the artery for which the clinical role is still unknown? Above all, will the late escapement of the restenotic process observed in the animal model have a clinical correlation when there is a longer follow up? It is still too soon to know if **paclitaxel** will raise the same questions. Indications not yet completely validated for the metallic endoprosthesis are disappearing little by little: acute infarction, long lesions. At last **restenosis** has been put in its proper place: the rate of re-intervention at 9 months remains less than 15% in the whole of the Presto study; systematic angiographic follow up at 6 months in the Trends study shows a **restenosis** rate of 13% on average. So the boundary between active **stent** and metallic **stent** seems more blurred than in 2001 when the results of the sirolimus studies were not available. The detection of ruptured or about to rupture plaque is a challenge which seems to be in hand now with techniques such as endocoronary echography or even more emergent techniques such as thermography, optical coherence tomography, or elastography. Which plaques should be treated? With medication? With mechanical tools? The work of the Lyon team on the clinical follow up of unstable plaques reveals a good prognosis for these plaques once the "guilty" lesion has been treated. The future of these techniques is thus perhaps more orientated towards primary prevention than towards secondary prevention.

CT Check Tags: Animal; Human
Coronary Angiography
*Coronary Arteriosclerosis: PP, physiopathology
*Coronary Arteriosclerosis: TH, therapy
***Coronary Restenosis**
Disease Models, Animal
Echocardiography
English Abstract
Inflammation
Preventive Medicine
Prognosis
Risk Factors
Rupture
Stents

L90 ANSWER 21 OF 55 MEDLINE on STN
AN 2003099915 MEDLINE
DN 22499742 PubMed ID: 12612382
TI **Taxol**-based eluting **stents** from theory to human validation: clinical and intravascular ultrasound observations.
AU Sonoda Shinjo; Honda Yasuhiro; Kataoka Toru; Bonneau Heidi N; Sudhir Krishnankutty; Yock Paul G; Mintz Gary S; Fitzgerald Peter J
CS Division of Cardiovascular Medicine, Stanford University Medical Center, California 94305, USA.
SO JOURNAL OF INVASIVE CARDIOLOGY, (2003 Mar) 15 (3) 109-14. Ref: 44
Journal code: 8917477. ISSN: 1042-3931.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200304
ED Entered STN: 20030304
Last Updated on STN: 20030425
Entered Medline: 20030424
AB Treatment with antiproliferative drugs via coated **stents** appears to be a promising approach to both mechanically remodel target lesions and biologically reduce neointimal hyperplasia. Drug-eluting **stents** can maximize local drug effects and minimize the potential for systemic toxic effects. The purpose of this review is to describe the effects of a

lipophilic microtubular inhibitor, **paclitaxel**, a strong antiproliferative agent under clinical investigation, and to define the vascular response to **taxol**-based eluting **stents** by intravascular ultrasound.

CT Check Tags: Human
*Angiogenesis Inhibitors: PD, pharmacology
*Angiogenesis Inhibitors: TU, therapeutic use
Blood Vessel Prosthesis Implantation
Cardiac Surgical Procedures
Clinical Trials
*Coated Materials, Biocompatible: PD, pharmacology
*Coated Materials, Biocompatible: TU, therapeutic use
Coronary Restenosis: PC, prevention & control
Coronary Restenosis: US, ultrasonography
***Paclitaxel: PD, pharmacology**
***Paclitaxel: TU, therapeutic use**
Reproducibility of Results
***Stents**
Ultrasonography, Interventional

RN **33069-62-4 (Paclitaxel)**
CN 0 (Angiogenesis Inhibitors); 0 (Coated Materials, Biocompatible)

L90 ANSWER 22 OF 55 MEDLINE on STN
AN 2003068588 MEDLINE
DN 22466654 PubMed ID: 12578884
TI Local drug delivery via a coronary **stent** with programmable release pharmacokinetics.
AU Finkelstein Ariel; McClean Dougal; Kar Saibal; Takizawa Kaname; Varghese Kiron; Baek Namjin; Park Kinam; Fishbein Michael C; Makkar Raj; Litvack Frank; Eigler Neal L
CS Division of Cardiology, Cedars-Sinai Medical Center and Department of Pathology at UCLA School of Medicine, 90048, USA.
SO CIRCULATION, (2003 Feb 11) 107 (5) 777-84.
Journal code: 0147763. ISSN: 1524-4539.
CY United States
DT (EVALUATION STUDIES)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200302
ED Entered STN: 20030212
Last Updated on STN: 20030227
Entered Medline: 20030226
AB BACKGROUND: Fixed drug release kinetics and vessel wall partitioning may limit the effectiveness of drug-eluting **stents**. We report preliminary experience using a new coronary **stent** with programmable pharmacokinetics. METHODS AND RESULTS: A newly designed metallic **stent** contains honeycombed strut elements with inlaid stacked layers of drug and polymer. In vitro studies evaluated recipes for loading **paclitaxel** to establish the parameters for controlling drug release. Manipulation of the layers of biodegradable polymer and drug allowed varying of the initial 24-hour burst release of **paclitaxel** from 69% to 8.6% (P<0.0001). Late release of drug could be adjusted dependently or independently of early burst release. A biphasic release profile was created by the addition of blank layers of polymer within the stack. In the 30-day porcine coronary model (n=17 pigs), there was a 70% reduction in late loss (0.3+/-0.5 versus 1.0+/-0.5 mm, P=0.04), a 28% increase in luminal volume (132+/-12 versus 103+/-21 mm(3), P=0.02), and a 50% decrease in histological neointimal area (2.0+/-0.5 versus 4.0+/-1.6 mm(2); P<0.001) compared with bare metal controls. Temporal and regional variations in vascular healing were seen histologically. CONCLUSIONS: Layered polymer/drug inlay **stent** technology permits flexible and controllable pharmacokinetic profiles.

Programmable, complex chemotherapy using this approach may be feasible for the treatment of cardiovascular disease.

CT Check Tags: Animal
Cell Division: DE, drug effects
Coated Materials, Biocompatible: PK, pharmacokinetics
Coronary Restenosis: PA, pathology
***Coronary Restenosis: PC, prevention & control**
Coronary Vessels: DE, drug effects
Coronary Vessels: PA, pathology
Coronary Vessels: SU, surgery
*Delayed-Action Preparations: PK, pharmacokinetics
*Drug Implants: PK, pharmacokinetics
Drug Implants: ST, standards
Equipment Design
Models, Animal
***Paclitaxel: PK, pharmacokinetics**
***Stents**
Stents: AE, adverse effects
Stents: ST, standards
Swine
Treatment Outcome
Tunica Intima: DE, drug effects
Tunica Intima: PA, pathology
Ultrasonography, Interventional
Vascular Patency: DE, drug effects

RN **33069-62-4 (Paclitaxel)**

CN 0 (Coated Materials, Biocompatible); 0 (Delayed-Action Preparations); 0 (Drug Implants)

L90 ANSWER 23 OF 55 MEDLINE on STN

AN 2003055832 MEDLINE

DN 22453155 PubMed ID: 12566366

TI TAXUS III Trial: in-**stent restenosis** treated with **stent**-based delivery of **paclitaxel** incorporated in a slow-release polymer formulation.

AU Tanabe Kengo; Serruys Patrick W; Grube Eberhard; Smits Pieter C; Selbach Guido; van der Giessen Willem J; Staberock Manfred; de Feyter Pim; Muller Ralf; Regar Evelyn; Degertekin Muzaffer; Ligthart Jurgen M R; Disco Clemens; Backx Bianca; Russell Mary E

CS Division of Cardiology, Thoraxcenter, Erasmus MC, Rotterdam, The Netherlands.

SO CIRCULATION, (2003 Feb 4) 107 (4) 559-64.
Journal code: 0147763. ISSN: 1524-4539.

CY United States

DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 200302

ED Entered STN: 20030205
Last Updated on STN: 20030214
Entered Medline: 20030213

AB BACKGROUND: The first clinical study of **paclitaxel**-eluting **stent** for de novo lesions showed promising results. We performed the TAXUS III trial to evaluate the feasibility and safety of **paclitaxel**-eluting **stent** for the treatment of in-**stent restenosis** (ISR). METHODS AND RESULTS: The TAXUS III trial was a single-arm, 2-center study that enrolled 28 patients with ISR meeting the criteria of lesion length < or =30 mm, 50% to 99% diameter stenosis, and vessel diameter 3.0 to 3.5 mm. They were treated with one or more TAXUS NIRx **paclitaxel**-eluting **stents**.
Twenty-five patients completed the angiographic follow-up at 6 months, and

17 of these underwent intravascular ultrasound (IVUS) examination. No subacute **stent** thrombosis occurred up to 12 months, but there was one late chronic total occlusion, and additional 3 patients showed angiographic **restenosis**. The mean late loss was 0.54 mm, with neointimal hyperplasia volume of 20.3 mm3. The major adverse cardiac event rate was 29% (8 patients; 1 non-Q-wave myocardial infarction, 1 coronary artery bypass grafting, and 6 target lesion revascularization [TLR]). Of the patients with TLR, 1 had **restenosis** in a bare **stent** implanted for edge dissection and 2 had **restenosis** in a gap between 2 **paclitaxel**-eluting **stents**. Two patients without angiographic **restenosis** underwent TLR as a result of the IVUS assessment at follow-up (1 incomplete apposition and 1 insufficient expansion of the **stent**). CONCLUSIONS: **Paclitaxel**-eluting **stent** implantation is considered safe and potentially efficacious in the treatment of ISR. IVUS guidance to ensure good **stent** deployment with complete coverage of target lesion may reduce reintervention.

CT Check Tags: Female; Human; Male
Antineoplastic Agents, Phytogenic: AD, administration & dosage
Coronary Angiography
Coronary Restenosis: DI, diagnosis
Coronary Restenosis: PC, prevention & control
***Coronary Restenosis: TH, therapy**
*Delayed-Action Preparations: AD, administration & dosage
Drug Implants: AD, administration & dosage
Drug Implants: AE, adverse effects
Feasibility Studies
Follow-Up Studies
Middle Age
***Paclitaxel: AD, administration & dosage**
*Polymers
***Stents**
Stents: AE, adverse effects
Treatment Outcome

RN **33069-62-4 (Paclitaxel)**

CN 0 (Antineoplastic Agents, Phytogenic); 0 (Delayed-Action Preparations); 0 (Drug Implants); 0 (Polymers)

L90 ANSWER 24 OF 55 MEDLINE on STN
AN 2003055826 MEDLINE
DN 22453148 PubMed ID: 12566359
TI **Paclitaxel** coating reduces in-**stent** intimal hyperplasia in human coronary arteries: a serial volumetric intravascular ultrasound analysis from the Asian **Paclitaxel**-Eluting **Stent** Clinical Trial (ASPECT).
CM Comment in: N Engl J Med. 2003 May 29;348(22):2254
AU Hong Myeong-Ki; Mintz Gary S; Lee Cheol Whan; Song Jong-Min; Han Ki-Hoon; Kang Duk-Hyun; Song Jae-Kwan; Kim Jae-Joong; Weissman Neil J; Fearnot Neal E; Park Seong-Wook; Park Seung-Jung
CS Department of Medicine, University of Ulsan College of Medicine, Songpa-gu, Seoul, Korea. (ASian Paclitaxel-Eluting Stent Clinical Trial).
SO CIRCULATION, (2003 Feb 4) 107 (4) 517-20.
Journal code: 0147763. ISSN: 1524-4539.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200302
ED Entered STN: 20030205
Last Updated on STN: 20030214
Entered Medline: 20030213

AB BACKGROUND: The aim of this study was to use serial volumetric intravascular ultrasound (IVUS) to evaluate the effect of a **paclitaxel** coating on in-**stent** intimal hyperplasia (IH). METHODS AND RESULTS: Patients were randomized to placebo (bare metal **stents**) or 1 of 2 doses of **paclitaxel** (low dose: 1.28 microg/mm2; high dose: 3.10 microg/mm2). Complete post-**stent** implantation and follow-up IVUS were available in 81 patients, including 25 control patients and in 28 receiving a low-dose and 28 receiving a high dose. Volumetric analysis of the **stented** segment and of both reference segments was performed. Baseline **stent** measurements and both reference measurements were similar among the groups. With increasing doses, there was a stepwise reduction in IH accumulation within the **stented** segment (31+/-22 mm3 in control, 18+/-15 mm3 in low dose, and 13+/-14 mm3 in high dose, P<0.001). Post hoc analysis showed less IH accumulation when low- and high-dose patients were compared with control (P=0.009 and P<0.001, respectively), but not when low-dose patients were compared with high-dose patients (P=0.2). Focal late malapposition was seen in 1 high-dose patient. With increasing doses, there was no significant change in the reference segments. CONCLUSIONS: **Paclitaxel**-coated **stents** are effective in reducing in-**stent** neointimal tissue proliferation in humans. They are not associated with edge **restenosis** or significant late malapposition.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
Cell Division: DE, drug effects
*Coated Materials, Biocompatible
Coated Materials, Biocompatible: AE, adverse effects
Coronary Arteriosclerosis: SU, surgery
*Coronary Arteriosclerosis: US, ultrasonography
Coronary Restenosis: ET, etiology
***Coronary Restenosis: PC, prevention & control**
Coronary Restenosis: US, ultrasonography
Dose-Response Relationship, Drug
Drug Implants: AD, administration & dosage
Follow-Up Studies
*Hyperplasia: PC, prevention & control
Hyperplasia: US, ultrasonography
Middle Age
***Paclitaxel: AD, administration & dosage**
***Stents**
Stents: AE, adverse effects
Treatment Outcome
Tunica Intima: DE, drug effects
Tunica Intima: US, ultrasonography
Ultrasonography, Interventional

RN **33069-62-4 (Paclitaxel)**
CN 0 (Coated Materials, Biocompatible); 0 (Drug Implants)

L90 ANSWER 25 OF 55 MEDLINE on STN
AN 2003031919 MEDLINE
DN 22226501 PubMed ID: 12241533
TI Human internal mammary artery organ culture model of coronary **stenting**: a novel investigation of smooth muscle cell response to drug-eluting **stents**.
AU Swanson Neil; Javed Qamar; Hogrefe Kai; Gershlick Anthony
CS Clinical Sciences Department, Glenfield Hospital, Leicester LE3 9QP, UK.. ns56@le.ac.uk
SO CLINICAL SCIENCE, (2002 Oct) 103 (4) 347-53.
Journal code: 7905731. ISSN: 0143-5221.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals

EM 200303
ED Entered STN: 20030124
Last Updated on STN: 20030321
Entered Medline: 20030320
AB Local drug delivery by coronary **stents** is of current research interest. Organ culture of human vascular tissue is a model of intimal hyperplasia. We report an ex vivo organ culture model of **stented** vessels. This allows **stent**-artery interactions to be studied in living tissue. The recognized anti-**restenosis** agent **paclitaxel** was chosen to test the organ culture model. Mammary artery specimens were cultured 'closed' (i.e. without opening them flat) for 72 h. Phosphocholine-coated **stents**, half of them loaded with the anti-**restenosis** drug **paclitaxel**, were implanted. The absorption and elution characteristics of **paclitaxel** were established. Artery tissue remained viable at 72 h when cultured closed, despite **stent** implantation. Specimens developed smooth muscle cell proliferation. The **stents** absorbed up to 127+/-29 microg of **paclitaxel**, with a biphasic elution curve. A mean of 13% of the absorbed **paclitaxel** remained after a 24 h perfusion. In mammary artery, these **paclitaxel** **stents** reduced or abolished smooth muscle cell proliferation compared with controls. This model allows the effects of **stenting** on human arterial tissue to be studied for at least 72 h, long enough to demonstrate effects on smooth muscle cell proliferation. Phosphocholine-coated **stents** absorb adequate doses of **paclitaxel**, which is eluted gradually, inhibiting muscle cell proliferation. Such an organ culture model of **stented** mammary artery will provide useful data in addition to that from animal or cell culture models of drug-eluting **stents**.
CT Check Tags: Human; In Vitro; Support, Non-U.S. Gov't
Cell Division: DE, drug effects
Coated Materials, Biocompatible
*Coronary Arteriosclerosis: PA, pathology
Drug Delivery Systems
Graft Occlusion, Vascular: PC, prevention & control
Mammary Arteries: ME, metabolism
*Models, Cardiovascular
Muscle, Smooth, Vascular: CY, cytology
*Muscle, Smooth, Vascular: ME, metabolism
Organ Culture: MT, methods
***Paclitaxel: PK, pharmacokinetics**
Phosphorylcholine
Recurrence
***Stents**
RN 107-73-3 (Phosphorylcholine); **33069-62-4 (Paclitaxel)**
CN 0 (Coated Materials, Biocompatible)

L90 ANSWER 26 OF 55 MEDLINE on STN
AN 2003029513 MEDLINE
DN 22424371 PubMed ID: 12537084
TI Drug-eluting **stents** to prevent reblockage of coronary arteries.
AU Schwertz Dorie W; Vaitkus Paul
CS Department of Medical Surgical Nursing, University of Illinois, Chicago, Illinois, USA.
SO JOURNAL OF CARDIOVASCULAR NURSING, (2003 Jan-Mar) 18 (1) 11-6. Ref: 23
Journal code: 8703516. ISSN: 0889-4655.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals; Nursing Journals
EM 200302

ED Entered STN: 20030123
Last Updated on STN: 20030214
Entered Medline: 20030212

AB **Restenosis** limits the success of percutaneous transluminal coronary interventions. Coronary artery **stenting** decreases **restenosis**, improves outcomes, and is currently the most commonly used percutaneous coronary intervention in the United States. However, in-**stent restenosis** continues to occur at an unacceptable rate. In-**stent restenosis** is a neointimal hyperplastic response resulting primarily from vascular smooth muscle cell proliferation. Treatment with anti-proliferative agents presents a logical approach to eradicating **restenosis**, however, these drugs are highly toxic. Coating **stents** with anti-proliferative agents allows local delivery of high doses and avoids systemic side effects. In 2001, the results of two clinical trials, RAVEL and ELUTES, using sirolimus- and paclitaxil-coated **stents** demonstrated nearly complete elimination of in-**stent restenosis**. These dramatic results represent a tremendous advance in the treatment of coronary heart disease.

CT Check Tags: Human
***Angioplasty, Transluminal, Percutaneous Coronary: IS, instrumentation**
Antineoplastic Agents: PD, pharmacology
Antineoplastic Agents: TU, therapeutic use
*Coated Materials, Biocompatible
Coronary Restenosis: PP, physiopathology
***Coronary Restenosis: PC, prevention & control**
Paclitaxel: PD, pharmacology
Paclitaxel: TU, therapeutic use
Sirolimus: PD, pharmacology
Sirolimus: TU, therapeutic use
***Stents**
Stents: AE, adverse effects

RN **33069-62-4 (Paclitaxel)**; 53123-88-9 (Sirolimus)

CN 0 (Antineoplastic Agents); 0 (Coated Materials, Biocompatible)

L90 ANSWER 27 OF 55 MEDLINE on STN

AN 2003009485 MEDLINE

DN 22403761 PubMed ID: 12515740

TI TAXUS I: six- and twelve-month results from a randomized, double-blind trial on a slow-release **paclitaxel**-eluting **stent** for de novo coronary lesions.

AU Grube Eberhard; Silber Sigmund; Hauptmann Karl Eugen; Mueller Ralf; Buellesfeld Lutz; Gerckens Ulrich; Russell Mary E

CS Department of Cardiology/Angiology, Heart Center Siegburg, Siegburg, Germany.. GrubeE@aol.com

SO CIRCULATION, (2003 Jan 7) 107 (1) 38-42.
Journal code: 0147763. ISSN: 1524-4539.

CY United States

DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 200301

ED Entered STN: 20030108
Last Updated on STN: 20030115
Entered Medline: 20030114

AB BACKGROUND: The TAXUS NIRx **stent** (Boston Scientific Corp) provides local delivery of **paclitaxel** via a slow-release polymer coating. The TAXUS I trial was the first in-human experience evaluating safety and feasibility of the TAXUS NIRx **stent** system compared

with bare NIR **stents** (control) (Boston Scientific Corp) for treatment of coronary lesions. METHODS AND RESULTS: METHODS AND RESULTS: The TAXUS I trial was a prospective, double-blind, three-center study randomizing 61 patients with de novo or restenotic lesions (< or =12 mm) to receive a TAXUS (n=31) versus control (n=30) **stent** (diameter 3.0 or 3.5 mm). Demographics, lesion characteristics, clinical outcomes were comparable between the groups. The 30-day major adverse cardiac event (MACE) rate was 0% in both groups (P=NS). No **stent** thromboses were reported at 1, 6, 9, or 12 months. At 12 months, the MACE rate was 3% (1 event) in the TAXUS group and 10% (4 events in 3 patients) in the control group (P=NS). Six-month angiographic **restenosis** rates were 0% for TAXUS versus 10% for control (P=NS) patients. There were significant improvements in minimal lumen diameter (2.60+/-0.49 versus 2.19+/-0.65 mm), diameter stenosis (13.56+/-11.77 versus 27.23+/-16.69), and late lumen loss (0.36+/-0.48 versus 0.71+/-0.48 mm) in the TAXUS group (all P<0.01). No evidence of edge **restenosis** was seen in either group. Intravascular ultrasound analysis showed significant improvements in normalized neointimal hyperplasia in the TAXUS (14.8 mm3) group compared with the control group (21.6 mm3) (P<0.05). CONCLUSIONS: In this feasibility trial, the TAXUS slow-release **stent** was well tolerated and showed promise for treatment of coronary lesions, with significant reductions in angiographic and intravascular ultrasound measures of **restenosis.**

CT Check Tags: Comparative Study; Female; Human; Male; Support, Non-U.S. Gov't
Aged
Coronary Angiography
Coronary Arteriosclerosis: DI, diagnosis
*Coronary Arteriosclerosis: DT, drug therapy
Coronary Arteriosclerosis: SU, surgery
Coronary Restenosis: EP, epidemiology
***Coronary Restenosis: PC, prevention & control**
Coronary Thrombosis: EP, epidemiology
Coronary Vessels: US, ultrasonography
Demography
Double-Blind Method
Drug Implants
Feasibility Studies
Follow-Up Studies
Middle Age
***Paclitaxel: AD, administration & dosage**
Paclitaxel: AE, adverse effects
Paclitaxel: TU, therapeutic use
***Stents**
Stents: AE, adverse effects

RN **33069-62-4 (Paclitaxel)**
CN 0 (Drug Implants)

L90 ANSWER 28 OF 55 MEDLINE on STN
AN 2003000145 MEDLINE
DN 22366560 PubMed ID: 12478230
TI Drug-eluting **stents**: role of **stent** design, delivery vehicle, and drug selection.
AU Rodgers Campbell D K
CS Cardiac Catheterization Laboratory, Brigham and Women's Hospital, Boston, Massachusetts, USA.
SO Rev Cardiovasc Med, (2002) 3 Suppl 5 S10-5.
Journal code: 100960007. ISSN: 1530-6550.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200301

ED Entered STN: 20030102
Last Updated on STN: 20030129
Entered Medline: 20030128
AB Increasing focus has recently been directed toward the different parameters of drug-eluting **stents-stent** design, delivery-vehicle materials, and drug properties-and the manner in which each of these elements may affect the function of the **stents**. Several specific characteristics of design may affect **restenosis**, although design optimization often presents a choice between acute procedural success and long-term biological stability. The influence of design parameters such as strut thickness and cell configuration is described. Polymer material has frequently been used to coat drug-eluting **stents**, although some agents, such as **paclitaxel**, can be attached directly to the **stent**'s surface, obviating the need for a polymer layer. The properties of agents used in drug-eluting **stents** and how those properties affect delivery and long-term outcome are discussed, as is the influence of the disease state of the target vessel on **stent** safety and efficacy.
CT Biocompatible Materials: CH, chemistry
*Coronary Disease: DT, drug therapy
Coronary Restenosis: PC, prevention & control
*Drug Delivery Systems: IS, instrumentation
Equipment Design
*Pharmaceutical Preparations: AN, analysis
Polymers: CH, chemistry
***Stents**
CN 0 (Biocompatible Materials); 0 (Pharmaceutical Preparations); 0 (Polymers)

L90 ANSWER 29 OF 55 MEDLINE on STN
AN 2002716365 MEDLINE
DN 22366563 PubMed ID: 12478233
TI Clinical experience with drug-eluting **stents**.
AU Drachman Douglas E
CS Department of Medicine, (Knight Cardiac Catheterization Laboratory, Cardiovascular Division, Massachusetts General Hospital) Harvard Medical School, Boston, Massachusetts, USA.
SO Rev Cardiovasc Med, (2002) 3 Suppl 5 S31-7. Ref: 21
Journal code: 100960007. ISSN: 1530-6550.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
LA English
FS Priority Journals
EM 200301
ED Entered STN: 20021217
Last Updated on STN: 20030129
Entered Medline: 20030128
AB Despite dramatic improvements in catheter and **stent** technology, **in-stent restenosis** continues to hamper initial procedural success in 10% to 50% of patients undergoing coronary intervention. Recent breakthroughs in polymer science and local drug delivery have shown tremendous promise in the long-sought-after goal of delivering antirestenotic therapy directly from a **stent**. Clinical trials examining several novel antirestenotic agents, particularly sirolimus and **paclitaxel**, have shown astonishing reduction in **restenosis** following **stenting**. Through examination of the clinical experience to date, we may gain insight into the current and future utility of drug-eluting **stents** in our clinical practice.
CT Check Tags: Comparative Study; Human
Angiogenesis Inhibitors: TU, therapeutic use
Clinical Trials

***Coronary Restenosis: PC, prevention & control**
*Drug Delivery Systems: IS, instrumentation
Immunosuppressive Agents: TU, therapeutic use
Paclitaxel: TU, therapeutic use
Polymers: CH, chemistry
Sirolimus: TU, therapeutic use
***Stents**
Treatment Outcome
RN **33069-62-4 (Paclitaxel)**; 53123-88-9 (Sirolimus)
CN 0 (Angiogenesis Inhibitors); 0 (Immunosuppressive Agents); 0 (Polymers)

L90 ANSWER 30 OF 55 MEDLINE on STN
AN 2002715160 MEDLINE
DN 22365089 PubMed ID: 12476650
TI Initial experience with **paclitaxel**-coated **stents**.
AU Grube Eberhard; Bullesfeld Lutz
CS Heart-Center Siegburg, Ringstrasse 49, 53721 Siegburg, Germany..
GrubeE@aol.com
SO JOURNAL OF INTERVENTIONAL CARDIOLOGY, (2002 Dec) 15 (6) 471-5. Ref: 20
Journal code: 8907826. ISSN: 0896-4327.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
LA English
FS Priority Journals
EM 200302
ED Entered STN: 20021217
Last Updated on STN: 20030207
Entered Medline: 20030206
AB Local delivery of immunosuppressive or antiproliferative agents using a drug-eluting **stent** is a new technology that is supposed to inhibit in-**stent restenosis**, thus providing a biological and mechanical solution. This technique is a very promising. To date, several agents have been used, including **paclitaxel**, QP-2, rapamycin, actinomycin D, dexamethason, tacrolimus, and everolimus. Several studies, published recently or still ongoing, have evaluated these drugs as to their release kinetics, effective dosage, safety in clinical practice, and benefit. These studies include: SCORE (**paclitaxel** derivative), TAXUS I-VI, ELUTES, ASPECT, DELIVER (**paclitaxel**), RAVEL, SIRIUS (sirolimus), ACTION (actinomycin), EVIDENT, PRESENT (tacrolimus), EMPEROR (dexamethason), and FUTURE (everolimus). **Paclitaxel** was one of the first **stent**-based antiproliferative agents under clinical investigation that provided profound inhibition of neointimal thickening depending on delivery duration and drug dosage. The randomized, multicenter SCORE trail (Quanam **stent**, **paclitaxel**-coated) enrolled 266 patients at 17 sites. At 6-month's follow-up, a drop of 83% in **stent restenosis** using the drug-eluting **stent** could be achieved (6.4% drug-eluting **stent** vs 36.9% control group), which was attributable to a remarkable decrease in intimal proliferation. Unfortunately, due to frequent **stent** thrombosis and side-branch occlusions, the reported 30-day MACE rate was 10.2%. The randomized TAXUS-I safety trial (BSC, NIRx, **paclitaxel**-coated) also demonstrated beneficial reduction of restenotic lesions at 6-month's follow-up (0% vs 10%) but was associated with the absence of thrombotic events presumably due to less drug dosage. The ongoing TAXUS II-VI trials are addressing additional insight regarding the efficacy of the TAXUS **paclitaxel**-eluting **stent**. ASPECT and ELUTES evaluated **paclitaxel**-coated **stents** (i.e., Cook and Supra G), including subgroups with different drug dosages. With respect to **stent restenosis** and neointimal proliferation, both studies demonstrated a clear dose response. The RAVEL and the SIRIUS

trials evaluated sirolimus-coated **stents** (i.e., Cordis, Johnson & Johnson, and Bx VELOCITY **stents**). Results confirmed the beneficial findings regarding reduction of renarrowing using a drug-eluting **stent** without any major adverse effects. Although parameters such as drug toxicity, optimal drug dosage, or delayed endothelial healing still need to be evaluated, today's clinical experience indicates that drug-coated **stents** are extremely beneficial in the interventional treatment of coronary lesions.

CT Check Tags: Human
Clinical Trials
***Coronary Restenosis: PC, prevention & control**
*Drug Delivery Systems: IS, instrumentation
*Growth Inhibitors: AD, administration & dosage
Growth Inhibitors: AE, adverse effects
***Paclitaxel: AD, administration & dosage**
Paclitaxel: AE, adverse effects
***Stents**

RN **33069-62-4 (Paclitaxel)**
CN 0 (Growth Inhibitors)

L90 ANSWER 31 OF 55 MEDLINE on STN
AN 2002677902 MEDLINE
DN 22325864 PubMed ID: 12438288
TI Mechanism of late in-**stent restenosis** after implantation of a **paclitaxel** derivate-eluting polymer **stent** system in humans.
AU Virmani Renu; Liistro Francesco; Stankovic Goran; Di Mario Carlo; Montorfano Matteo; Farb Andrew; Kolodgie Frank D; Colombo Antonio
CS Catheterization Laboratories, Ospedale San Raffaele and Emo Centro Cuore Columbus, Milan, Italy.. virmani@afip.osd.mil
SO CIRCULATION, (2002 Nov 19) 106 (21) 2649-51.
Journal code: 0147763. ISSN: 1524-4539.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200211
ED Entered STN: 20021120
Last Updated on STN: 20021213
Entered Medline: 20021125
AB BACKGROUND: We recently reported delayed angiographic **restenosis** in 15 patients who received 7-hexanoyltaxol (QP2)-eluting polymer **stents** (QuaDS) for the treatment of in-**stent restenosis**. This study presents the histological findings of atherectomy specimens from a subset of these patients receiving implants. METHODS AND RESULTS: Between October and December 2001, 5 patients treated with QuaDS-QP2 **stents** underwent directional coronary atherectomy at 11.2+/-1.0 months for recurrent in-**stent restenosis**. Restenotic lesion composition was assessed with special stains, immunohistochemistry with quantitative image analysis, and, in one specimen, transmission electron microscopy. Atherectomy specimens contained fibrin interspersed in a smooth muscle cell-rich neointima with proteoglycan matrix. In 2 of 5 specimens, large aggregates of macrophages and T-lymphocytes were noted. These areas of active inflammation demonstrated a relatively high proliferation index by Ki-67 antibody staining, whereas the proliferation index in smooth muscle cell-rich restenotic areas was low. CONCLUSION: Restenotic lesions from QuaDS-QP2-eluting **stents** at 12 months show persistent fibrin deposition with varying degrees of inflammation. These pathological changes, representing delayed healing, are usually observed up to only 3 months in human coronary arteries with stainless steel balloon-expandable **stents**. The nonreabsorbable polymer alone may have induced

chronic inflammation.
CT Check Tags: Female; Human; Male
Aged
Atherectomy, Coronary
Blood Vessel Prosthesis Implantation: AE, adverse effects
Bridged Compounds: AD, administration & dosage
*Bridged Compounds: AE, adverse effects
Chronic Disease
Coronary Angiography
Coronary Arteriosclerosis: PA, pathology
Coronary Arteriosclerosis: SU, surgery
Coronary Restenosis: DI, diagnosis
***Coronary Restenosis: ET, etiology**
Coronary Restenosis: SU, surgery
Coronary Vessels: PA, pathology
Coronary Vessels: SU, surgery
*Delayed-Action Preparations: AE, adverse effects
*Drug Implants: AE, adverse effects
Inflammation: ET, etiology
Inflammation: PA, pathology
Middle Age
Mitotic Index
*Polymers: AE, adverse effects
Recurrence
Reoperation
***Stents: AE, adverse effects**
CN 0 (7-hexanoyltaxol); 0 (Bridged Compounds); 0 (Delayed-Action Preparations); 0 (Drug Implants); 0 (Polymers)

L90 ANSWER 32 OF 55 MEDLINE on STN
AN 2002627633 MEDLINE
DN 22272996 PubMed ID: 12385349
TI Drug eluting **stents**: managing coronary artery stenosis following PTCA.
AU Garces Kirsten
SO Issues Emerg Health Technol, (2002 Oct) (40) 1-6.
Journal code: 100886782. ISSN: 1488-6324.
CY Canada
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Health Technology
EM 200210
ED Entered STN: 20021019
Last Updated on STN: 20021029
Entered Medline: 20021028
AB Drug eluting **stents** (DES) release drugs that inhibit tissue growth in narrowed coronary arteries in an effort to prevent **restenosis**, a renarrowing of the artery. Several types of DES are under investigation in clinical trials; however, none are currently approved for use in Canada. Preliminary trial data are encouraging, demonstrating greater lumen diameter and reduced **restenosis** with DES versus uncoated **stents**. If DES prove to be more effective than uncoated **stents** in the treatment and/or prevention of **restenosis**, this technology may diffuse rapidly. The total health care costs, including the cost of the **stents**, post-intervention therapy and possible re-intervention costs, will require assessment to determine the ultimate impact of DES.
CT Check Tags: Human
***Angioplasty, Transluminal, Percutaneous Coronary: AE, adverse effects**
Canada
Clinical Trials
*Constriction, Pathologic

Coronary Disease: DT, drug therapy
Coronary Vessels: PA, pathology
Cost-Benefit Analysis
Drug Approval
Drug Delivery Systems
Europe
European Union
Paclitaxel
Sirolimus
***Stents**
Stents: AE, adverse effects
Stents: EC, economics
Treatment Outcome
RN **33069-62-4 (Paclitaxel)**; 53123-88-9 (Sirolimus)

L90 ANSWER 33 OF 55 MEDLINE on STN
AN 2002626774 MEDLINE
DN 22272188 PubMed ID: 12384629
TI Drug-eluting **stents**: clinical experiences and perspectives.
AU Grube E; Gerckens U; Buellesfeld L
CS Heart Center Siegburg, Siegburg, Germany, Italy.. GrubeE@aol.com
SO MINERVA CARDIOANGIOLOGICA, (2002 Oct) 50 (5) 469-73. Ref: 8
Journal code: 0400725. ISSN: 0026-4725.
CY Italy
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200301
ED Entered STN: 20021018
Last Updated on STN: 20030122
Entered Medline: 20030121
AB Drug-eluting **stents** (DES) have entered the arena and are about to changed the landscape of Interventional Cardiology. Today, the number of agents under preclinical and clinical investigation has increased considerably, including drugs such as **Paclitaxel**, Sirolimus, Tacrolimus, Everolimus, Dexamethasone, etc. Several studies have recently been published or are still ongoing evaluating different **stent** designs with respect to their safety and efficacy in treatment of coronary lesions. The SCORE trial (**Paclitaxel**) revealed a significant reduction in **restenosis** at follow-up (FU) in the drug-eluting **stent** group (6.4% vs 36.9% control group), attributable to decreased intimal proliferation. However, **stentthromboses** and myocardial infarctions, due to both **stent** design and high drug dosages, were observed causing a MACE rate of 10.2% in the DES group. Confirming the beneficial reduction of **stent** renarrowing using a local drug-eluting device, the rate of **restenosis** in the TAXUS-I trial (**Paclitaxel**) was 0% at follow-up in patients with DES vs 10% in patients with bare **stents**. Differences in MACE were not observed, which underlined the potential impact of an optimal **stent** design. First clinical experiences with a Sirolimus-coated **stent** (FIM trial) demonstrated again a profound inhibition of neointimal ingrowth at 4-month follow-up. The RAVEL trial, the first multicenter trial evaluating the Sirolimus **stent** and the largest DES study published so far, confirmed the FIM findings with a rate of **restenosis** in the DES group of 0% at 6 month FU. At 12 month FU, the beneficial impact on neointimal growth inhibition was persistent. The pivotal study SIRIUS is addressed to evaluate this **stent** design more extensively. However, given all the results being available today, local application of anti-proliferative agents delivered by coronary **stents** is one of the most promising techniques in treatment of coronary lesions. Nevertheless, we need more trials and an agreement of

definitions in order to evaluate this treatment concept and eliminate unwanted side-effects.
CT Check Tags: Comparative Study; Human
Angiogenesis Inhibitors
***Angioplasty, Transluminal, Percutaneous Coronary**
Antibiotics, Macrolide
*Coated Materials, Biocompatible
*Coronary Arteriosclerosis: TH, therapy
***Coronary Restenosis: PC, prevention & control**
Follow-Up Studies
Immunosuppressive Agents
Multicenter Studies
Paclitaxel
*Pharmaceutical Preparations
Randomized Controlled Trials
Safety
Sirolimus
***Stents**
Time Factors
RN **33069-62-4 (Paclitaxel)**; 53123-88-9 (Sirolimus)
CN 0 (Angiogenesis Inhibitors); 0 (Antibiotics, Macrolide); 0 (Coated Materials, Biocompatible); 0 (Immunosuppressive Agents); 0 (Pharmaceutical Preparations)

L90 ANSWER 34 OF 55 MEDLINE on STN
AN 2002626771 MEDLINE
DN 22272185 PubMed ID: 12384626
TI Drug-eluting **stent**: the emerging technique for the prevention of **restenosis**.
AU Sheiban I; Carrieri L; Catuzzo B; Destefanis P; Oliaro E; Moretti C; Trevi G P
CS Interventional Cardiology, Division of Cardiology, San Giovanni Battista Hospital, University of Turin, Turin, Italy.. isheiban@yahoo.com
SO MINERVA CARDIOANGIOLOGICA, (2002 Oct) 50 (5) 443-53. Ref: 69
Journal code: 0400725. ISSN: 0026-4725.
CY Italy
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200301
ED Entered STN: 20021018
Last Updated on STN: 20030122
Entered Medline: 20030121
AB Percutaneous coronary interventions (PCI) have surpassed coronary artery bypass grafting as the most common means for treating coronary artery disease, because of materials improvement, the use of **stent** and pharmacotherapy. However, despite the variety of mechanical techniques such as dilatation, debulking or conventional **stent** implantation, the incidence of **restenosis** on short and mid-term follow-up is still representing an important limitation to PCI. **Restenosis** is mainly due to elastic recoil, negative vessel remodelling and neointimal proliferation, as a response to vessel injury induced by angioplasty devices. The use of conventional **stents** has provided an efficient method to avoid elastic recoil and negative vessel remodelling, thus partially reducing **restenosis** as compared to conventional balloon dilatation. However, neointimal proliferation (biological vessel response to injury caused by **stent** implantation) is not affected by **stenting** technique. Thus, the extensive use of coronary **stent**, even in complex lesions, have produced again a "new" disease: the in-**stent** **restenosis** especially in some patients' subset (diabetics) or in

some lesion subset (bifurcations, long lesions, small vessels, total occlusions, diffuse disease). Therefore, the main target of today's interventional cardiologists is to resolve this problem. The combination between mechanical control of elastic recoil and negative remodelling (**stent**) and the control of neointimal proliferation - biological response to vessel injury - (antiproliferative drugs) is the emerging approach against **restenosis**. This emerging approach consists in using the **stent** as drug carrier to the target site. Local delivery of antiproliferative or immunosuppressive agents using a drug-coated **stent** is supposed to inhibit in **stent restenosis**. The first antiproliferative agents being used successfully in clinical trials are sirolimus and **paclitaxel** and, so far, the data available of these trials demonstrated a marked reduction of **restenosis** using sirolimus- and **paclitaxel** -coated **stents** as compared to conventional **stents**. However, many questions are still to be answered and several other clinical trials with drug-eluting **stents** are ongoing, evaluating safety and efficacy of sirolimus and **paclitaxel** in a larger number of patients and in different subset of coronary lesions type and morphology. Based on the very impressive results available at the present time, we can expect, in the very near future, remarkable changes in our clinical practice and the beginning of a new "era" of interventional cardiology.

CT Check Tags: Comparative Study; Human
Angiogenesis Inhibitors
***Angioplasty, Transluminal, Percutaneous Coronary**
Antibiotics, Macrolide
Clinical Trials
***Coronary Restenosis: PC, prevention & control**
Immunosuppressive Agents
Multicenter Studies
Paclitaxel
*Pharmaceutical Preparations
Prospective Studies
Randomized Controlled Trials
Sirolimus
***Stents**
Time Factors

RN **33069-62-4 (Paclitaxel)**; 53123-88-9 (Sirolimus)

CN 0 (Angiogenesis Inhibitors); 0 (Antibiotics, Macrolide); 0 (Immunosuppressive Agents); 0 (Pharmaceutical Preparations)

L90 ANSWER 35 OF 55 MEDLINE on STN

AN 2002626770 MEDLINE

DN 22272184 PubMed ID: 12384625

TI [Drug-eluting **stents** do they make the difference?]. Gli **stent** ricoperti di farmaci fanno davvero la differenza?.

AU Presbitero P; Asioli M

CS Laboratorio di Emodinamica e Cardiologia Interventistica, Istituto di Clinica Humanitas, Rozzano, Milan, Italy.

SO MINERVA CARDIOANGIOLOGICA, (2002 Oct) 50 (5) 431-42. Ref: 39
Journal code: 0400725. ISSN: 0026-4725.

CY Italy

DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)

LA Italian

FS Priority Journals

EM 200301

ED Entered STN: 20021018
Last Updated on STN: 20030122
Entered Medline: 20030121

AB The main limitation to further expansion of PTCI (percutaneous

transluminal coronary intervention) is **restenosis** that occurs in 30% of the patients within 6-months after the procedure. Coronary **stenting** decreases the percent of **restenosis** due to arterial remodeling after PTCI but proliferation of **smooth muscle cells** due to **vascular** injury still remains. A mechanical approach the only treatment up to now (further balloon expansion, plaque removal with rotablator or directional atherectomy) failed. Because the restenotic process is due to a complex series of biological events which start with platelet aggregation, grow-factors and cytochine release, the use of antiflammatory, antithrombotic and antiproliferative drugs were attempted. Cortisone and heparin showed low benefits in clinical trial. New drugs (rapamycin, **taxol**, actinomycin D, tacrolimus, estradiol, dexamethazone) with antiproliferative and antiflammatory activities are under evaluation. They act as inhibitors of the **cell migration** and of the **cell** cicle progression with different specific molecular mechanisms. The first pilot study performed in 45 patients with sirolimus-eluting **stents** has shown a sustained suppression (25% in the fast release group and 23% in the slow release group) of neointimal formation at 12 months after procedure with absence of **restenosis** . The Ravel study, a randomized trial, has enrolled 238 patients treated with sirolimus coated **stent** vs a control group: the results confirm the previous data with a complete suppression of intimal hyperproliferation and **restenosis** at six months follow-up. The first 400 patients treated in the Sirius trial a similar study which will randomize 1100 pts show a low, but not a complete inhibition of the restenotic process probably due to a more complexity of the lesions treated in comparison to Ravel trial (9.2% of **restenosis**). Another very promising drug is **taxol (paclitaxel)**. It is an antiproliferative and antinflammatory molecule tested in a series of clinical trials called Taxus. The still unpublished data of TAXUS I and TAXUS II randomized trial show extremely low **restenosis** rate. Other drugs (actinomycin D, estradiol, tacrolimus, dexamethazone) show to have a potential effect on **restenosis** and neointimal proliferation and are under investigation. Is very important to maintain lessons learned from the past. The design, the type, the **smooth** surface of the **stent** still remains very important as it is a good expansion and a full coverage of the lesions with a "good **stent**" in the attempt to reduce **restenosis**. Drug-eluting **stents** will add further improvement.

CT Check Tags: Comparative Study; Support, Non-U.S. Gov't
Angiogenesis Inhibitors
***Angioplasty, Transluminal, Percutaneous Coronary**
Clinical Trials
Coated Materials, Biocompatible
***Coronary Restenosis: PC, prevention & control**
English Abstract
Estradiol
***Graft Occlusion, Vascular: PC, prevention & control**
Immunosuppressive Agents
Multicenter Studies
Paclitaxel
*Pharmaceutical Preparations
Pilot Projects
Randomized Controlled Trials
***Stents**
Tacrolimus
Time Factors

RN 109581-93-3 (Tacrolimus); **33069-62-4 (Paclitaxel)**; 50-28-2 (Estradiol)

CN 0 (Angiogenesis Inhibitors); 0 (Coated Materials, Biocompatible); 0 (Immunosuppressive Agents); 0 (Pharmaceutical Preparations)

L90 ANSWER 36 OF 55 MEDLINE on STN
AN 2002626769 MEDLINE
DN 22272183 PubMed ID: 12384624
TI Drug-eluting **stents.**
AU Chieffo A; Colombo A
CS Interventional Cardiology EMO, Centro Cuore Columbus and San Raffaele Hospital, Milan, Italy.
SO MINERVA CARDIOANGIOLOGICA, (2002 Oct) 50 (5) 419-29. Ref: 41
Journal code: 0400725. ISSN: 0026-4725.
CY Italy
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200301
ED Entered STN: 20021018
Last Updated on STN: 20030122
Entered Medline: 20030121
AB Drug-eluting **stents** represent the third revolution in the field of Interventional Cardiology following balloon angioplasty (PTCA) and the implantation of metal **stents.** The main limitation of percutaneous coronary intervention (PCI) is **restenosis.** The introduction of drug eluting **stents** able to release antiproliferative compounds led to the evaluation of several antiproliferative drugs in order to reduce **restenosis.** Rapamycin (Sirolimus) has been demonstrated to inhibit smooth muscle cell (SMC) proliferation and migration in vitro and to reduce in vivo neointima formation with blockage of the cell cycle progression at the G1-S transition. In a pilot study, recently confirmed by a randomized trial, rapamycin drug-eluting **stents** have been reported to eliminate **restenosis** after **stent** implantation. Promising data also come from the use of **paclitaxel** drug-eluting **stents** . **Paclitaxel** (**Taxol**) is a microtubule-stabilizing agent with potent antiproliferative activity. Even if drug-eluting **stents** represent one of the most promising fields in Interventional Cardiology today before being sure of their real potential it is necessary to wait for results from several ongoing clinical studies, their usage in real-world lesions and extended follow-up to 5 years.
CT Check Tags: Comparative Study; Human
***Angioplasty, Transluminal, Percutaneous Coronary**
*Antibiotics, Macrolide
Clinical Trials
Coated Materials, Biocompatible
Coronary Angiography
***Coronary Restenosis: PC, prevention & control**
Follow-Up Studies
Forecasting
***Graft Occlusion, Vascular: PC, prevention & control**
*Immunosuppressive Agents
***Paclitaxel**
Pilot Projects
Randomized Controlled Trials
*Sirolimus
***Stents**
Time Factors
RN **33069-62-4 (Paclitaxel);** 53123-88-9 (Sirolimus)
CN 0 (Antibiotics, Macrolide); 0 (Coated Materials, Biocompatible); 0 (Immunosuppressive Agents)

L90 ANSWER 37 OF 55 MEDLINE on STN
AN 2002620576 MEDLINE
DN 22265377 PubMed ID: 12378395

TI [State of treatment of coronary artery disease by drug releasing **stents**].
Aktueller Stand der Therapie der koronaren Herzkrankheit mit medikamentenbeschichteten **Stents**.
AU Muller Ralf; Bullesfeld Lutz; Gerckens Ulrich; Grube Eberhard
CS Abteilung fur Kardologie, Herzzentrum Siegburg, Germany.. Rmueller@KHSU.de
SO HERZ, (2002 Sep) 27 (6) 508-13. Ref: 18
Journal code: 7801231. ISSN: 0340-9937.
CY Germany: Germany, Federal Republic of
DT (EVALUATION STUDIES)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA German
FS Priority Journals
EM 200302
ED Entered STN: 20021017
Last Updated on STN: 20030221
Entered Medline: 20030219
AB BACKGROUND: Despite improved technologies **restenosis** remains the main drawback of catheter-based interventions in coronary artery disease. Local application of anti-proliferative drugs through drug releasing **stents** is a promising concept addressed to solve this problem. DRUG RELEASING **STENTS**: Today, given the technical capabilities for controlled drug release from coronary **stents**, the development of drug eluting **stents** has emerged as one of the main research areas in interventional cardiovascular medicine. Several different approaches for drug loading on coronary **stents** as well as a variety of antiproliferative and anti-inflammatory agents, such as **paclitaxel**, actinomycin D, sirolimus, tacrolimus, everolimus and dexamethasone are under clinical investigation. RESULTS: Since the first enthusiastic reports from first in-man observations with drug coated **stents**, the success of the combination of both a biological and a mechanical approach has been proved in several controlled studies with **restenosis** rates between 0% in the RAVEL trial (sirolimus, Cordis Bx Velocity trade mark **stent**), 0% in the TAXUS I trial (**paclitaxel**, Boston Scientific NIRx trade mark **stent**) and 4% in the ASPECT Study (**paclitaxel**, Cook V-Flex plus trade mark **stent**). The risk of **stent** thrombosis seems to depend on the dose of the antiproliferative drug - in the SCORE trial **stent** thrombosis occurred in 6.3% of patients with high dose of QP2 and the antiplatelet therapy, in the ASPECT subgroup with cilostazol instead of clopidogrel and high dose of **paclitaxel** in up to 25%, whereas in RAVEL and TAXUS I no **stent** thrombosis was observed. CONCLUSION: If the "one digit" **restenosis** rate observed in clinical trials could be confirmed in clinical practice without increase of complications, especially **stent** thrombosis using multiple and/or long **stents**, we can expect in the near future that implanting drug eluting **stents** in larger patient groups and lesion subsets will cause a reduction of patients with need for surgical revascularization.
CT Check Tags: Comparative Study; Human
***Angioplasty, Transluminal, Percutaneous Coronary: IS, instrumentation**
*Anti-Inflammatory Agents: AD, administration & dosage
*Cell Division: DE, drug effects
*Coated Materials, Biocompatible
*Coronary Disease: TH, therapy
*Drug Carriers
English Abstract
*Immunosuppressive Agents: PD, pharmacology
Randomized Controlled Trials
***Stents**
Treatment Outcome

CN 0 (Anti-Inflammatory Agents); 0 (Coated Materials, Biocompatible); 0 (Drug Carriers); 0 (Immunosuppressive Agents)

L90 ANSWER 38 OF 55 MEDLINE on STN
AN 2002495379 MEDLINE
DN 22243984 PubMed ID: 12357129
TI Can we prevent in-**stent restenosis**?.
AU Garza Luis; Aude Y Wady; Saucedo Jorge F
CS Division of Cardiovascular Medicine, University of Arkansas for Medical Sciences, Little Rock, 72205, USA.. garzaluis@uams.edu
SO CURRENT OPINION IN CARDIOLOGY, (2002 Sep) 17 (5) 518-25. Ref: 90
Journal code: 8608087. ISSN: 0268-4705.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200303
ED Entered STN: 20021002
Last Updated on STN: 20030306
Entered Medline: 20030305
AB Nowadays **stent** placement has replaced balloon angioplasty as the most commonly performed percutaneous coronary interventional procedure, mainly because of its better acute and chronic outcome. As a result, in-**stent restenosis** (ISR) has become a widespread problem.
The incidence of ISR varies from 10% to 50% and depends on the absence or presence of several risk factors, such as small vessel size, longer lesions, and diabetes. Intravascular ultrasound studies have demonstrated that ISR is mainly caused by neointimal proliferation; consequently, this pathologic process has become the target of many preventive and therapeutic approaches. This article provides an overview of such management strategies, highlighting the rather disappointing experiences with mechanical and systemic drug therapies; the relative merits and disadvantages of intracoronary radiation; and the exciting yet realistic promise, embodied by the recent advancements in drug-eluting **stent** technology, of potentially eradicating ISR in the near future.
CT Check Tags: Animal; Human
Angioplasty, Transluminal, Percutaneous Coronary
Brachytherapy
Cell Cycle: DE, drug effects
Coated Materials, Biocompatible: AD, administration & dosage
*Coronary Disease: TH, therapy
Coronary Restenosis: PP, physiopathology
***Coronary Restenosis: PC, prevention & control**
Drug Delivery Systems
Gene Transfer Techniques
Paclitaxel: AD, administration & dosage
Paclitaxel: TU, therapeutic use
Sirolimus: AD, administration & dosage
Sirolimus: PD, pharmacology
Sirolimus: TU, therapeutic use
***Stents: AE, adverse effects**
RN **33069-62-4 (Paclitaxel)**; 53123-88-9 (Sirolimus)
CN 0 (Coated Materials, Biocompatible)

L90 ANSWER 39 OF 55 MEDLINE on STN
AN 2002453169 MEDLINE
DN 22197607 PubMed ID: 12208792
TI Sustained reduction of in-**stent** neointimal growth with the use of a novel systemic nanoparticle **paclitaxel**.
AU Kolodgie Frank D; John Michael; Khurana Charanjit; Farb Andrew; Wilson Patricia S; Acampado Eduardo; Desai Neil; Soon-Shiong Patrick; Virmani

Renu
CS Department of Cardiovascular Pathology, Armed Forces Institute of Pathology, Washington, DC 20306, USA.
SO CIRCULATION, (2002 Sep 3) 106 (10) 1195-8.
Journal code: 0147763. ISSN: 1524-4539.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200209
ED Entered STN: 20020906
Last Updated on STN: 20020910
Entered Medline: 20020909
AB BACKGROUND: **Paclitaxel** (PXL)-eluting **stents** in animals cause incomplete healing and, in some instances, a lack of sustained suppression of neointimal growth. The present study tested the efficacy of a novel systemic delivery nanoparticle PXL for reducing in-**stent restenosis**. METHODS AND RESULTS: A saline-reconstituted formulation of PXL stabilized by albumin nanoparticles (nPXL) was tested in 38 New Zealand White rabbits receiving bilateral iliac artery **stents**. Doses of nPXL (1.0 to 5.0 mg/kg) were administered as a 10-minute intra-arterial infusion; control animals received vehicle (0.9% normal saline). In a follow-up chronic experiment, nPXL 5.0 mg/kg was given at **stenting** with or without an intravenous 3.5-mg/kg repeat nPXL dose at 28 days; these studies were terminated at 3 months. At 28 days, mean neointimal thickness was reduced (P< or =0.02) by doses of nPXL > or =2.5 mg/kg with evidence of delayed healing. The efficacy of a single dose of nPXL 5.0 mg/kg, however, was lost by 90 days. In contrast, a second repeat dose of nPXL 3.5 mg/kg given 28 days after **stenting** resulted in sustained suppression of neointimal thickness at 90 days (P< or =0.009 versus single dose nPXL 5.0 mg/kg and controls) with nearly complete neointimal healing. CONCLUSIONS: Although systemic nPXL reduces neointimal growth at 28 days, a single repeat dose was required for sustained neointimal suppression. Thus, this novel systemic formulation of PXL may allow adjustment of dose at the **stent** treatment site and prove to be a useful adjunct for the clinical prevention of in-**stent restenosis**.
CT Check Tags: Animal; Male
Angiogenesis Inhibitors: AD, administration & dosage
Angiogenesis Inhibitors: PK, pharmacokinetics
*Angiogenesis Inhibitors: TU, therapeutic use
Arteries: PA, pathology
Arteries: UL, ultrastructure
***Graft Occlusion, Vascular: DT, drug therapy**
Graft Occlusion, Vascular: ET, etiology
Graft Occlusion, Vascular: ME, metabolism
Graft Occlusion, Vascular: PA, pathology
Kinetics
Leukocyte Count
Paclitaxel: AD, administration & dosage
Paclitaxel: PK, pharmacokinetics
***Paclitaxel: TU, therapeutic use**
Particle Size
Rabbits
***Stents: AE, adverse effects**
RN **33069-62-4 (Paclitaxel)**
CN 0 (Angiogenesis Inhibitors)

L90 ANSWER 40 OF 55 MEDLINE on STN
AN 2002257610 MEDLINE
DN 21992652 PubMed ID: 11997271
TI First clinical experience with a **paclitaxel** derivate-eluting polymer **stent** system implantation for in-**stent**

restenosis: immediate and long-term clinical and angiographic outcome.

AU Liistro Francesco; Stankovic Goran; Di Mario Carlo; Takagi Takuro; Chieffo Alaide; Moshiri Shahram; Montorfano Matteo; Carlino Mauro; Briguori Carlo; Pagnotta Paolo; Albiero Remo; Corvaja Nicola; Colombo Antonio
CS Catheterization Laboratories, Ospedale San Raffaele, and Emo Centro Cuore Columbus, Milan, Italy.

SO CIRCULATION, (2002 Apr 23) 105 (16) 1883-6.
Journal code: 0147763. ISSN: 1524-4539.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200205
ED Entered STN: 20020509
Last Updated on STN: 20020517
Entered Medline: 20020516

AB BACKGROUND: It has been shown that antiproliferative drugs such as **paclitaxel** lower the amount of intimal hyperplasia after **stent** implantation. We report the first clinical experience of 7-hexanoyltaxol (QP2)-eluting polymer **stent** system (QuaDS) implantation for in-**stent restenosis**. METHODS AND RESULTS: Fifteen consecutive patients with elective indication to percutaneous coronary intervention for in-**stent restenosis** were treated with the QuaDS-QP2 **stent** implantation. The QuaDS-QP2 **stent** was successfully implanted in all but 2 target lesions. In one lesion, the restenotic segment could not be completely covered by the **stent**, and in another lesion, a bare metal **stent** was implanted distally to the QuaDS-QP2 **stent**. One patient suffered from postprocedural non-Q-wave myocardial infarction (NQWMI). No other adverse events were observed during hospital stay. Six- and 12-month angiographic and clinical follow-up was scheduled for all patients. At 6 months, 3 patients had target lesion revascularization (20%). Two patients had **restenosis** (13.3%); one experienced **restenosis** in a gap between 2 drug-eluting **stents**, and the other had **stent** occlusion leading to NQWMI. Minimal intimal hyperplasia was observed in all the segments covered by drug-eluting **stents** (late loss=0.47+/-1.01 mm with a loss index=0.17+/-0.39). At 12 months, 1 patient suffered from NQWMI, and 8 of 13 patients (61.5%) had angiographic **restenosis** (late loss=1.36+/-0.94 mm with a loss index=0.62+/-0.44). CONCLUSION: This first experience with QuaDS-QP2 **stent** implantation for in-**stent restenosis** revealed minimal intimal hyperplasia at the 6-month follow-up. However, the antiproliferative effect was not maintained at the 12-month follow-up, resulting in delayed occurrence of angiographic **restenosis**.

CT Check Tags: Case Report; Female; Human; Male; Support, Non-U.S. Gov't
Bridged Compounds: AD, administration & dosage
*Bridged Compounds: TU, therapeutic use
Coronary Angiography
Drug Implants
Follow-Up Studies
***Graft Occlusion, Vascular: DT, drug therapy**
Graft Occlusion, Vascular: ET, etiology
Graft Occlusion, Vascular: RA, radiography
Growth Inhibitors: AD, administration & dosage
Growth Inhibitors: TU, therapeutic use
Middle Age
Polymers: AD, administration & dosage
Polymers: TU, therapeutic use
***Stents**
Stents: AE, adverse effects

Treatment Outcome
CN 0 (7-hexanoyltaxol); 0 (Bridged Compounds); 0 (Drug Implants); 0 (Growth Inhibitors); 0 (Polymers)

L90 ANSWER 41 OF 55 MEDLINE on STN
AN 2002215817 MEDLINE
DN 21949369 PubMed ID: 11951791
TI Histopathologic alterations after endovascular radiation and antiproliferative **stents**: similarities and differences.
AU Virmani Renu; Farb Andrew; Kolodgie Frank D
CS Department of Cardiovascular Pathology, Armed Forces Institute of Pathology, Washington, DC, USA.. virmani@afip.osd.mil
SO HERZ, (2002 Feb) 27 (1) 1-6. Ref: 34
Journal code: 7801231. ISSN: 0340-9937.
CY Germany: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200205
ED Entered STN: 20020416
Last Updated on STN: 20020522
Entered Medline: 20020520
AB BACKGROUND: Endovascular radiation and drug-eluting antiproliferative **stents** in experimental animals (normal pigs and rabbit arteries) show a decrease in the neointimal growth at 1 month vs. controls. However, this is accompanied by delayed healing characterized by persistence of neointimal fibrin (with or without inflammation), a decrease in smooth muscle cells, and incomplete endothelialization. Conversely, stainless steel control **stents** show complete healing with the neointima consisting of smooth muscle cells in a proteoglycan-collagen matrix and near complete luminal surface endothelialization. RESULTS: Long-term (3 and 6 months) animal studies fail to show any benefit with radiation or drug-eluting **stents**. These experimental results are discrepant from those seen clinically in man where both therapies have shown benefit at 6 months, suggesting that animal data may not be predictive of clinical results. The main differences can be explained on the basis of preclinical studies performed in juvenile animals without underlying atherosclerosis, which leads to accelerated healing in animals vs. man such that 1 month animal data likely correspond to 6 months in man. Therefore long-term (24-30 months) angiographic and/or IVUS follow-up studies in man will be required to determine if drug-eluting **stents** will behave similarly to animal studies at 3 and 6 months.
CT Check Tags: Animal; Comparative Study; Human
*Antineoplastic Agents, Phytogenic: AD, administration & dosage
Antineoplastic Agents, Phytogenic: PD, pharmacology
*Brachytherapy
***Coronary Restenosis: PC, prevention & control**
*Coronary Vessels: PA, pathology
Fibrin: ME, metabolism
Follow-Up Studies
*Iliac Artery: PA, pathology
*Inflammation: PA, pathology
Microscopy, Electron, Scanning
***Paclitaxel: AD, administration & dosage**
Paclitaxel: PD, pharmacology
Platelet Aggregation
Rabbits
*Radiation-Sensitizing Agents: AD, administration & dosage
Radiation-Sensitizing Agents: PD, pharmacology
Stainless Steel

***Stents**
Stents: AE, adverse effects
Swine
Thrombosis: PA, pathology
RN 12597-68-1 (Stainless Steel); **33069-62-4 (Paclitaxel)**; 9001-31-4 (Fibrin)
CN 0 (Antineoplastic Agents, Phytogenic); 0 (Radiation-Sensitizing Agents)

L90 ANSWER 42 OF 55 MEDLINE on STN
AN 2002136067 MEDLINE
DN 21685818 PubMed ID: 11827699
TI Local delivery of low-dose docetaxel, a novel microtubule polymerizing agent, reduces neointimal hyperplasia in a balloon-injured rabbit iliac artery model.
CM Comment in: Cardiovasc Res. 2002 Feb 1;53(2):292-3
AU Yasuda Satoshi; Noguchi Teruo; Gohda Masahiro; Arai Takashi; Tsutsui Nobumasa; Nakayama Yasuhide; Matsuda Takehisa; Nonogi Hiroshi
CS National Cardiovascular Center, Division of Cardiology, Department of Medicine, 5-7-1 Fujishiro-dai, Suita, Osaka 565-8565, Japan.. syasuda@hsp.ncvc.go.jp
SO CARDIOVASCULAR RESEARCH, (2002 Feb 1) 53 (2) 481-6.
Journal code: 0077427. ISSN: 0008-6363.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200203
ED Entered STN: 20020302
Last Updated on STN: 20020312
Entered Medline: 20020311
AB OBJECTIVE: Docetaxel (DOC) is a novel microtubule polymerizing agent, with superior antiproliferative properties as compared to **paclitaxel**. DOC is therefore a potential therapeutic tool for the prevention of **restenosis** following angioplasty. However, DOC has systemic toxicity such as leukocytopenia, which occurs in a dose-dependent manner. To minimize such adverse effects, we carried out local delivery of low-dose DOC directly to injured vessel sites. METHODS: The rabbit iliac artery was denuded, and then DOC (2 mg) or control vehicle was administered locally 20 min, via a local drug delivery catheter. RESULTS: The levels of DOC in the plasma were within ng/ml range, eliminating hematopoietic side effects. Seven days after the local delivery (DOC: n=4, control: n=4), DOC decreased the number of Ki-67-labeled cells in the intima (DOC: 22 +/-10 vs. control: 66 +/- 18 cells/mm(2), P<0.01), indicating a decreased proliferative activity. At 28 days (DOC: n=8, control: n=8), computer-assisted morphometric analysis demonstrated that DOC significantly reduced the intimal area (DOC: 0.15 +/- 0.13 vs. control: 0.70 +/- 0.13 mm(2), P<0.01). There was also a decrease in medial area in the DOC-treated vessels (DOC: 0.62 +/- 0.17 vs. control: 1.13 +/- 0.38 mm(2), P<0.01). CONCLUSIONS: Local delivery of DOC, even after a single low-dose administration, effectively inhibits neointimal hyperplasia. Such administration is associated with a minimal likelihood of systemic adverse effects (leukocytopenia), but potentially induces local toxicity (a decrease in medial wall thickness) due to extensive cytotoxic effect.
CT Check Tags: Animal; Support, Non-U.S. Gov't
Administration, Topical
Analysis of Variance
Antineoplastic Agents: BL, blood
*Antineoplastic Agents: PD, pharmacology
***Balloon Dilatation: AE, adverse effects**
Drug Delivery Systems
Hyperplasia
Iliac Artery: PA, pathology

Image Processing, Computer-Assisted
Leukocyte Count
*Paclitaxel: AA, analogs & derivatives
Paclitaxel: BL, blood
*Paclitaxel: PD, pharmacology
Rabbits
*Tunica Intima: PA, pathology
RN 114977-28-5 (docetaxel); **33069-62-4 (Paclitaxel)**
CN 0 (Antineoplastic Agents)

L90 ANSWER 43 OF 55 MEDLINE on STN
AN 2002090892 MEDLINE
DN 21623392 PubMed ID: 11753151
TI Acute cardiac tolerance of current contrast media and the new taxane protaxel using iopromide as carrier during porcine coronary angiography and **stenting**.
AU Scheller Bruno; Speck Ulrich; Schmitt Alexander; Clauss Wolfam; Sovak Milos; Bohm Michael; Stoll Hans Peter
CS Internal Medicine III (Cardiology), University of Saarland, Homburg/Saar, Germany.. scheller@med-in.uni-saarland.de
SO INVESTIGATIVE RADIOLOGY, (2002 Jan) 37 (1) 29-34.
Journal code: 0045377. ISSN: 0020-9996.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200203
ED Entered STN: 20020201
Last Updated on STN: 20020326
Entered Medline: 20020325
AB RATIONALE AND OBJECTIVES: The systemic tolerance thresholds of modern low-osmolar x-ray contrast media (CM) are similarly high, but their effects on the cardiovascular system and on the coagulation differ. The aim of this study was to comparatively evaluate the cardiovascular tolerability of iopromide, ioxaglate, and iosmin, and of a novel taxane protaxel, dissolved in iopromide, as a carrier, by coronary angiography and **stenting**. METHODS: Sixteen pigs were randomized into four groups: iosmin (350 mg iodine/mL, n = 4, nonionic dimer), iopromide (370 mg iodine/mL, n = 4, nonionic monomer), ioxaglate (320 mg iodine/mL, n = 4, ionic dimer), and 70-micromol protaxel dissolved in iopromide 370 mg iodine/mL, intended to prevent **restenosis**. Coronary angiography was performed via the left carotid artery followed by implantation of **stents** into the left anterior descending and the circumflex arteries. About 80 mL per animal was used in each group. RESULTS: There were no thrombotic complications and no significant adverse events of electrocardiography, blood pressure, or contractility during or after CM injections. There were no differences among the CM tested except that ioxaglate was the only agent showing a significant reduction in dp/dt after 50 seconds compared to iosmin. The values of preinjection parameters were most rapidly regained after iosmin, compared with other CM tested. CONCLUSIONS: The novel iso-osmolar nonionic CM iosmin is well tolerated in porcine coronary angiography and subsequent **stenting**. The cardiac tolerance of iopromide has not been adversely affected by addition of the cytostatic protaxel.
CT Check Tags: Animal; Comparative Study; Support, Non-U.S. Gov't
*Contrast Media
Contrast Media: AE, adverse effects
*Coronary Angiography: MT, methods
Iodine: AE, adverse effects
Iodine: DU, diagnostic use
Iohexol: AE, adverse effects
*Iohexol: AA, analogs & derivatives
Iohexol: DU, diagnostic use

Ioxaglic Acid: AE, adverse effects
Ioxaglic Acid: DU, diagnostic use
Models, Animal
Paclitaxel: AE, adverse effects
***Paclitaxel: AA, analogs & derivatives**
Paclitaxel: DU, diagnostic use
Prodrugs: DU, diagnostic use
Stents
Swine
RN **33069-62-4 (Paclitaxel)**; 59017-64-0 (Ioxaglic Acid); 66108-95-0 (Iohexol); 73334-07-3 (iopromide); 7553-56-2 (Iodine)
CN 0 (Contrast Media); 0 (Prodrugs); 0 (iosmin); 0 (protaxel)

L90 ANSWER 44 OF 55 MEDLINE on STN
AN 2002045048 MEDLINE
DN 21628825 PubMed ID: 11756213
TI **Stent** development and local drug delivery.
AU Regar E; Sianos G; Serruys P W
CS Department of Cardiology, Thoraxcentre, Erasmus Medical Centre Rotterdam, The Netherlands.
SO BRITISH MEDICAL BULLETIN, (2001) 59 227-48. Ref: 78
Journal code: 0376542. ISSN: 0007-1420.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200202
ED Entered STN: 20020124
Last Updated on STN: 20020212
Entered Medline: 20020211
AB **Stent** implantation has become the new standard angioplasty procedure. In-**stent** re-stenosis remains the major limitation of coronary **stenting**. Re-stenosis is related to patient-, lesion- and procedure-specific factors. Patient-specific factors can not be influenced to any extent. Procedure-specific factors are affected by implantation technique and **stent** characteristics. Design and material influence vascular injury and humoral and cellular response. Radiation has been shown to have inhibitory effects on smooth muscle cell growth and neo-intima formation, but in clinical trials the outcome has been hampered by re-stenosis at the edges of the radioactive **stent** ('candy wrapper'). New approaches target pharmacological modulation of local vascular biology by local administration of drugs. This allows for drug application at the precise site and time of vessel injury. Systemic release is minimal and this may reduce the risk of toxicity. The drug and the delivery vehicle must fulfil pharmacological, pharmacokinetic and mechanical requirements and the application of eluting degradable matrices seems to be a possible solution. Numerous pharmacological agents with antiproliferative properties are currently under clinical investigation, e.g. actinomycin D, rapamycin or **paclitaxel**. Another approach is for **stents** to be made of biodegradable materials as an alternative to metallic **stents**. Their potential long-term complications, such as in-**stent** re-stenosis and the inaccessibility of the lesion site for surgical revascularization, needs to be assessed. Current investigational devices and the line of (pre)clinical investigation are discussed in detail. Currently, there is little experimental, and only preliminary clinical, understanding of the acute and long-term effects of drug-eluting or biodegradable **stents** in coronary arteries. The clinical benefit of these approaches still has to be proven.
CT Check Tags: Human; Support, Non-U.S. Gov't
Angioplasty, Transluminal, Percutaneous Coronary

Antibiotics: AD, administration & dosage
Antineoplastic Agents: AD, administration & dosage
Biodegradation
Coronary Restenosis: PC, prevention & control
Coronary Restenosis: TH, therapy
Dactinomycin: AD, administration & dosage
*Drug Delivery Systems
Equipment Design
Myocardial Ischemia: DT, drug therapy
*Myocardial Ischemia: TH, therapy
Paclitaxel: AD, administration & dosage
Protein Synthesis Inhibitors: AD, administration & dosage
Sirolimus: AD, administration & dosage
***Stents**

RN **33069-62-4 (Paclitaxel)**; 50-76-0 (Dactinomycin); 53123-88-9 (Sirolimus)
CN 0 (Antibiotics); 0 (Antineoplastic Agents); 0 (Protein Synthesis Inhibitors)

L90 ANSWER 45 OF 55 MEDLINE on STN
AN 2001669345 MEDLINE
DN 21553050 PubMed ID: 11696691
TI **Paclitaxel**-coated Gianturco-Roubin II (GR II) **stents** reduce neointimal hyperplasia in a porcine coronary in-**stent restenosis** model.
AU Hong M K; Kornowski R; Bramwell O; Ragheb A O; Leon M B
CS Cornell University, New York Presbyterian Hospital, New York 10021, USA.. mkh2003@med.cornell.edu
SO CORONARY ARTERY DISEASE, (2001 Sep) 12 (6) 513-5.
Journal code: 9011445. ISSN: 0954-6928.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200112
ED Entered STN: 20011122
Last Updated on STN: 20020123
Entered Medline: 20011213
AB BACKGROUND: Drug-coated **stents** may treat both mechanisms of **restenosis**, namely, geometric remodeling and neointimal hyperplasia. **Paclitaxel**, an antimicrotubule agent, has been shown to inhibit smooth muscle cell proliferation and migration, and may be an excellent candidate for local elution from a **stent** platform. METHODS: To study the **antirestenosis** effects of drug-coated **stents**, we impregnated **paclitaxel** (175-200 microg/**stent** with programmed elution over 6 months) on Gianturco-Roubin II (GR II) **stents**. These **stents** and control **stents** without drugs were implanted in porcine coronary arteries (**stent**/artery approx. 1.1) and evaluated 4 weeks later. RESULTS: The vessel size and the **stent**-to-artery ratio were similar between the groups. However, at 4 weeks, the **paclitaxel** group had significantly reduced in-**stent restenosis** compared with the controls (51 +/- 27 versus 27 +/- 27% diameter stenosis, $P < 0.05$ and 669 +/- 357 versus 403 +/- 197 microm neointimal thickness, $P < 0.05$). This study further confirmed the biocompatibility of the polymer, with no foreign body reaction in any of the groups. CONCLUSIONS: This study shows that the **paclitaxel**-coated **stents** significantly reduced in-**stent restenosis** without eliciting inflammation.
CT Check Tags: Animal; Support, Non-U.S. Gov't
*Angiogenesis Inhibitors: TU, therapeutic use
Coronary Angiography
Coronary Vessels: PA, pathology

Coronary Vessels: SU, surgery
Disease Models, Animal
Graft Occlusion, Vascular: PA, pathology
***Graft Occlusion, Vascular: PC, prevention & control**
Graft Occlusion, Vascular: RA, radiography
Hyperplasia: PA, pathology
Hyperplasia: PC, prevention & control
Hyperplasia: RA, radiography
***Paclitaxel: TU, therapeutic use**
***Stents**
Swine
*Tunica Intima: PA, pathology
Tunica Intima: RA, radiography
RN **33069-62-4 (Paclitaxel)**
CN 0 (Angiogenesis Inhibitors)

L90 ANSWER 46 OF 55 MEDLINE on STN
AN 2001431580 MEDLINE
DN 21371939 PubMed ID: 11479260
TI Physiological transport forces govern drug distribution for **stent**-based delivery.
AU Hwang C W; Wu D; Edelman E R
CS Harvard-MIT Division of Health Sciences and Technology, Massachusetts Institute of Technology, Cambridge, MA 02139, USA.. cwhwang@mit.edu
NC GM/HL-49039 (NIGMS)
HL-60407 (NHLBI)
SO CIRCULATION, (2001 Jul 31) 104 (5) 600-5.
Journal code: 0147763. ISSN: 1524-4539.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200109
ED Entered STN: 20010917
Last Updated on STN: 20010917
Entered Medline: 20010913
AB BACKGROUND: The first compounds considered for **stent**-based delivery, such as heparin, were chosen on the basis of promising tissue culture and animal experiments, and yet they have failed to stop **restenosis** clinically. More recent compounds, such as **paclitaxel**, are of a different sort, being hydrophobic in nature, and their effects after local release seem far more profound. This dichotomy raises the question of whether drugs that have an effect when released from a **stent** do so because of differences in biology or differences in physicochemical properties and targeting. METHODS AND RESULTS: We applied continuum pharmacokinetics to examine the effects of transport forces and device geometry on the distribution of **stent**-delivered hydrophilic and hydrophobic drugs. We found that **stent**-based delivery invariably leads to large concentration gradients, with drug concentrations ranging from nil to several times the mean tissue concentration over a few micrometers. Concentration variations were a function of the Peclet number (Pe), the ratio of convective to diffusive forces. Although hydrophobic drugs exhibited greater variability than hydrophilic drugs, they achieved higher mean concentrations and remained closer to the intima. Inhomogeneous strut placement influenced hydrophilic drugs more negatively than hydrophobic drugs, dramatically affecting local concentrations without changing mean concentrations. CONCLUSIONS: Because local concentrations and gradients are inextricably linked to biological effect, our results provide a potential explanation for the variable success of **stent**-based delivery. We conclude that mere proximity of delivery devices to tissues does not ensure adequate targeting, because physiological transport forces cause local concentrations to deviate significantly from mean concentrations.

CT Check Tags: Animal; In Vitro; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Biological Transport: DE, drug effects
*Biological Transport: PH, physiology
Carotid Arteries: ME, metabolism
Cattle
Dose-Response Relationship, Drug
*Drug Delivery Systems: MT, methods
Fluorescein: DU, diagnostic use
Microscopy, Fluorescence
Pharmaceutical Preparations: AD, administration & dosage
Pharmaceutical Preparations: CH, chemistry
*Pharmaceutical Preparations: ME, metabolism
***Stents**
RN 2321-07-5 (Fluorescein)
CN 0 (Pharmaceutical Preparations)

L90 ANSWER 47 OF 55 MEDLINE on STN
AN 2001420361 MEDLINE
DN 21361243 PubMed ID: 11468212
TI Pathological analysis of local delivery of **paclitaxel** via a polymer-coated **stent**.
AU Farb A; Heller P F; Shroff S; Cheng L; Kolodgie F D; Carter A J; Scott D S; Froehlich J; Virmani R
CS Department of Cardiovascular Pathology, Armed Forces Institute of Pathology, Washington, DC, USA.
SO CIRCULATION, (2001 Jul 24) 104 (4) 473-9.
Journal code: 0147763. ISSN: 1524-4539.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200109
ED Entered STN: 20010910
Last Updated on STN: 20010910
Entered Medline: 20010906
AB BACKGROUND: **Paclitaxel** can inhibit vascular smooth muscle proliferation in vitro, and early studies suggest that **paclitaxel** may be useful in preventing **restenosis**. Early and late intimal growth and local vascular pathological changes associated with **paclitaxel** delivered via **stents** have not been fully explored. METHODS AND RESULTS: Localized drug delivery was accomplished with balloon-expandable stainless steel **stents** coated with a cross-linked biodegradable polymer, chondroitin sulfate and gelatin (CSG), containing various doses of **paclitaxel**. CSG-coated **stents** with **paclitaxel** (42.0, 20.2, 8.6, or 1.5 microgram of **paclitaxel** per **stent**), CSG-coated **stents** without **paclitaxel**, and uncoated **stents** (without **paclitaxel** or CSG) were deployed in the iliac arteries of New Zealand White rabbits, which were killed 28 days after implant. Mean neointimal thickness at **stent** strut sites was reduced 49% ($P<0.0003$) and 36% ($P<0.007$) with **stents** containing 42.0 and 20.2 microgram of **paclitaxel** per **stent**, respectively, versus CSG-coated **stents** without **paclitaxel**. However, histological findings suggested incomplete healing in the higher-dose (42.0 and 20.2 microgram) **paclitaxel**-containing **stents** consisting of persistent intimal fibrin deposition, intraintimal hemorrhage, and increased intimal and adventitial inflammation. **Stents** coated with CSG alone (without **paclitaxel**) had similar neointimal growth as uncoated **stents**. In a separate group of rabbits killed at 90 days, neointimal growth was no longer suppressed by CSG-coated **stents** containing 42.0 or 21.0 microgram of **paclitaxel** CONCLUSIONS: CSG coating appears to be a

promising medium for localized drug delivery. **Paclitaxel** polymer-coated **stents** reduce neointima formation but are associated with evidence of incomplete healing at 28 days. However, neointimal suppression was not maintained at 90 days.

CT Check Tags: Animal; Male
Angiogenesis Inhibitors: PK, pharmacokinetics
*Angiogenesis Inhibitors: PD, pharmacology
Cell Division: DE, drug effects
Chondroitin Sulfates
Dose-Response Relationship, Drug
*Drug Delivery Systems: MT, methods
Fibrin: DE, drug effects
Fibrin: ME, metabolism
Gelatin
Hemorrhage: CI, chemically induced
Hemorrhage: PA, pathology
Iliac Artery: DE, drug effects
Iliac Artery: ME, metabolism
Iliac Artery: PA, pathology
Inflammation: CI, chemically induced
Inflammation: PA, pathology
Paclitaxel: BL, blood
Paclitaxel: PK, pharmacokinetics
***Paclitaxel: PD, pharmacology**
Polymers
Rabbits
***Stents**
Time Factors
Tunica Intima: DE, drug effects
Tunica Intima: ME, metabolism
Tunica Intima: PA, pathology

RN **33069-62-4 (Paclitaxel)**; 9000-70-8 (Gelatin); 9001-31-4 (Fibrin); 9007-28-7 (Chondroitin Sulfates)

CN 0 (Angiogenesis Inhibitors); 0 (Polymers)

L90 ANSWER 48 OF 55 MEDLINE on STN

AN 2001335098 MEDLINE

DN 21296080 PubMed ID: 11403421

TI Inhibition of smooth muscle cell proliferation after local drug delivery of the antimitotic drug **paclitaxel** using a porous balloon catheter.

AU Oberhoff M; Kunert W; Herdeg C; Kuttner A; Kranzhofer A; Horch B; Baumbach A; Karsch K R

CS Bristol Heart Institute, Bristol Royal Infirmary, University of Bristol, UK.. Martin.Oberhoff@bristol.ac.uk

SO BASIC RESEARCH IN CARDIOLOGY, (2001 May-Jun) 96 (3) 275-82. Journal code: 0360342. ISSN: 0300-8428.

CY Germany: Germany, Federal Republic of

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 200110

ED Entered STN: 20011029
Last Updated on STN: 20011029
Entered Medline: 20011025

AB Percutaneous transluminal coronary angioplasty is an accepted treatment for coronary artery disease. The major limitation, however, is the high incidence of **restenosis** which limits the long-term benefit of this intervention. **Paclitaxel** is a new antiproliferative agent that has generated considerable scientific interest since it was introduced in clinical trials in the early 1980s. Recent in vitro studies have shown that **paclitaxel** has considerable antiproliferative activity in human coculture systems. In the present study the efficacy of

paclitaxel was investigated after development of an intimal plaque by electrical stimulation and additional cholesterol diet and subsequent balloon angioplasty in 63 New Zealand White rabbits. Local drug delivery of **paclitaxel** was accomplished in 30 rabbits with a porous balloon catheter (35 holes, hole diameter 75 microm, 2.5 mm catheter diameter). **Paclitaxel** was administered locally with 4 ml (solution 10(-5) mol/L) using an injection pressure of 2 atmospheric To study the extent of **restenosis** and morphological changes, the animals were sacrificed 7, 28 or 56 days after intervention. After staining procedures quantification of SMC proliferation, intimal macrophages and morphological analyses were performed. **Paclitaxel** plasma concentrations were measured using HPLC technique. One week after balloon angioplasty the arteries treated with local **paclitaxel** delivery showed an insignificant trend towards a reduction in intimal smooth muscle cell proliferation (untreated 8.4 +/- 4.9 % vs **paclitaxel** treated 2.4 +/- 2.4 %, p = NS). However, this resulted in a significant reduction of stenosis degree of 66 % 8 weeks after intervention compared to the untreated group (untreated 41 +/- 18 % vs **paclitaxel** treated 14 +/- 11 %, p = 0.005). In conclusion, locally delivered **paclitaxel** prevented neointimal thickening in the rabbit carotid artery after balloon angioplasty. Local **paclitaxel** treatment may therefore be a clinical option for the prevention of **restenosis** after coronary interventions. However, further preclinical studies have to prove long-term efficacy and safety.

CT Check Tags: Animal; Comparative Study; Human; Male
Angioplasty, Transluminal, Percutaneous Coronary: IS, instrumentation
*Antineoplastic Agents: AD, administration & dosage
*Antineoplastic Agents: AI, antagonists & inhibitors
Antineoplastic Agents: BL, blood
***Balloon Dilatation**
Cell Count
Coronary Disease: TH, therapy
*Coronary Vessels: CY, cytology
*Coronary Vessels: DE, drug effects
*Drug Delivery Systems: IS, instrumentation
Endothelium: CY, cytology
Endothelium: DE, drug effects
Injections, Intramuscular: IS, instrumentation
Macrophages: DE, drug effects
Models, Animal
Models, Cardiovascular
*Muscle, Smooth, Vascular: CY, cytology
*Muscle, Smooth, Vascular: DE, drug effects
***Paclitaxel: AD, administration & dosage**
***Paclitaxel: AI, antagonists & inhibitors**
Paclitaxel: BL, blood
Rabbits
Severity of Illness Index
Time
Time Factors
Treatment Outcome
Tunica Intima: DE, drug effects
RN **33069-62-4 (Paclitaxel)**
CN 0 (Antineoplastic Agents)

L90 ANSWER 49 OF 55 MEDLINE on STN
AN 2001299719 MEDLINE
DN 21266747 PubMed ID: 11342479
TI **Paclitaxel stent** coating inhibits neointimal hyperplasia at 4 weeks in a porcine model of coronary **restenosis**.
AU Heldman A W; Cheng L; Jenkins G M; Heller P F; Kim D W; Ware M Jr; Nater

C; Hruban R H; Rezai B; Abella B S; Bunge K E; Kinsella J L; Sollott S J; Lakatta E G; Brinker J A; Hunter W L; Froehlich J P
CS Division of Cardiology, Department of Pathology, Johns Hopkins School of Medicine, Baltimore, Md, USA.. aheldman@jhmi.edu
SO CIRCULATION, (2001 May 8) 103 (18) 2289-95.
Journal code: 0147763. ISSN: 1524-4539.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200106
ED Entered STN: 20010618
Last Updated on STN: 20010618
Entered Medline: 20010614
AB BACKGROUND: Despite limiting elastic recoil and late **vascular** remodeling after angioplasty, coronary **stents** remain vulnerable to **restenosis**, caused primarily by neointimal hyperplasia. **Paclitaxel**, a microtubule-stabilizing drug, has been shown to inhibit **vascular smooth muscle cell migration** and proliferation contributing to neointimal hyperplasia. We tested whether **paclitaxel**-coated coronary **stents** are effective at preventing neointimal proliferation in a porcine model of **restenosis**. METHODS AND RESULTS: Palmaz-Schatz **stents** were dip-coated with **paclitaxel** (0, 0.2, 15, or 187 microgram/**stent**) by immersion in ethanolic **paclitaxel** and evaporation of the solvent. **Stents** were deployed with mild oversizing in the left anterior descending coronary artery (LAD) of 41 minipigs. The treatment effect was assessed 4 weeks after **stent** implantation. The angiographic late loss index (mean luminal diameter) decreased with increasing **paclitaxel** dose ($P<0.0028$ by ANOVA), declining by 84.3% (from 0.352 to 0.055, $P<0.05$) at the highest level tested (187 microgram/**stent** versus control). Accompanying this change, the neointimal area decreased (by 39.5%, high-dose versus control; $P<0.05$) with increasing dose ($P<0.040$ by ANOVA), whereas the luminal area increased (by 90.4%, high-dose versus control; $P<0.05$) with escalating dose ($P<0.0004$ by ANOVA). Inflammatory **cells** were seen infrequently, and there were no cases of aneurysm or thrombosis. CONCLUSIONS: **Paclitaxel**-coated coronary **stents** produced a significant dose-dependent inhibition of neointimal hyperplasia and luminal encroachment in the pig LAD 28 days after implantation; later effects require further study. These results demonstrate the potential therapeutic benefit of **paclitaxel**-coated coronary **stents** in the prevention and treatment of human coronary **restenosis**.
CT Check Tags: Animal; Female; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Coronary Angiography
Coronary Vessels: CH, chemistry
*Coronary Vessels: DE, drug effects
Coronary Vessels: SU, surgery
Disease Models, Animal
Dose-Response Relationship, Drug
Graft Occlusion, Vascular: PA, pathology
***Graft Occlusion, Vascular: PC, prevention & control**
Hyperplasia: PA, pathology
Hyperplasia: PC, prevention & control
Infusion Pumps, Implantable
***Paclitaxel: AD, administration & dosage**
Paclitaxel: AN, analysis
***Stents**
Surface Properties
Swine, Miniature
*Tunica Intima: DE, drug effects

Tunica Intima: PA, pathology
Tunica Intima: SU, surgery
RN **33069-62-4 (Paclitaxel)**

L90 ANSWER 50 OF 55 MEDLINE on STN
AN 2001256786 MEDLINE
DN 21040614 PubMed ID: 11200358
TI Complete inhibition of intimal hyperplasia by perivascular delivery of **paclitaxel** in balloon-injured rat carotid arteries.
AU Signore P E; Machan L S; Jackson J K; Burt H; Bromley P; Wilson J E; McManus B M
CS Angiotech Pharmaceuticals, Vancouver, BC, Canada.
SO JOURNAL OF VASCULAR AND INTERVENTIONAL RADIOLOGY, (2001 Jan) 12 (1) 79-88. Journal code: 9203369. ISSN: 1051-0443.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200105
ED Entered STN: 20010521
Last Updated on STN: 20010521
Entered Medline: 20010517
AB PURPOSE: To determine whether perivascular delivery of **paclitaxel** prevents luminal narrowing after balloon injury by inhibiting intimal hyperplasia. MATERIALS AND METHODS: Immediately after balloon injury of the entire left common carotid artery, three slow-release formulations of **paclitaxel** or control formulations without drug were applied around a distal segment of the artery. The noninjured right carotid arteries were evaluated as a control. The animals were maintained for 14 and 28 days (n = 5 in each group at each time interval). Histology, immunohistochemistry, and morphometric analysis were performed. RESULTS: Injured nontreated arteries exhibited a pronounced intimal hyperplasia (0.185 +/- 0.01 mm2 at 14 days and 0.189 +/- 0.01 mm2 at 28 days) and a marked reduction in luminal area (44% at 14 days and 43% at 28 days). Medial area and the number of medial cells increased by 44% and 45%, respectively, at 14 days, and by 22% and 37%, respectively, at 28 days. Injured arteries treated with perivascular **paclitaxel** did not show any intimal hyperplasia, and luminal area was increased in five of six groups and was unchanged in one group. These arteries had an increased medial area but they had fewer medial cells than noninjured arteries. Injured arteries treated with control implants without **paclitaxel** exhibited intimal hyperplasia and luminal narrowing. CONCLUSION: Perivascular slow release of **paclitaxel** totally inhibits intimal hyperplasia and prevents luminal narrowing after balloon injury. Because of its efficacy, perivascular **paclitaxel** represents a possible approach for prevention of **restenosis** in humans.
CT Check Tags: Animal; Support, Non-U.S. Gov't
*Angiogenesis Inhibitors: TU, therapeutic use
***Angioplasty, Balloon: AE, adverse effects**
Carotid Artery, Common: DE, drug effects
*Carotid Artery, Common: PA, pathology
Hyperplasia
***Paclitaxel: TU, therapeutic use**
Rats
Rats, Wistar
Tunica Intima: DE, drug effects
*Tunica Intima: PA, pathology
RN **33069-62-4 (Paclitaxel)**
CN 0 (Angiogenesis Inhibitors)

L90 ANSWER 51 OF 55 MEDLINE on STN
AN 2001077309 MEDLINE

DN 21013372 PubMed ID: 11127480
TI Neointimal thickening after **stent** delivery of **paclitaxel** : change in composition and arrest of growth over six months.
CM Comment in: J Am Coll Cardiol. 2001 Jul;38(1):292-3
AU Drachman D E; Edelman E R; Seifert P; Groothuis A R; Bornstein D A; Kamath K R; Palasis M; Yang D; Nott S H; Rogers C
CS Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts 02115, USA.. ddrachman@partners.org
NC GM/HL 49039 (NIGMS)
HL 03104 (NHLBI)
HL 60407 (NHLBI)
SO JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY, (2000 Dec) 36 (7) 2325-32. Journal code: 8301365. ISSN: 0735-1097.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200101
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010111
AB OBJECTIVES: The purpose of this study was to determine long-term effects of **stent**-based **paclitaxel** delivery on amount, rate and composition of neointimal thickening after **stent** implantation. BACKGROUND: **Paclitaxel** prevents **vascular smooth muscle cell** proliferation and **migration** in vitro and in vivo. These actions, coupled with low solubility, make it a viable candidate for modulating **vascular** responses to injury and prolonged effects after local delivery. We asked whether local delivery of **paclitaxel** for a period of weeks from a **stent** coated with a bioerodible polymer could produce a sustained reduction in neointimal hyperplasia for up to six months after **stenting**. METHODS: Stainless steel **stents** were implanted in the iliac arteries of rabbits after endothelial denudation. **Stents** were uncoated or coated with a thin layer of poly(lactide-co-sigma-caprolactone) copolymer alone or containing **paclitaxel**, 200 microg. RESULTS: **Paclitaxel** release in vitro followed first-order kinetics for two months. Tissue responses were examined 7, 28, 56 or 180 days after implantation. **Paclitaxel** reduced intimal and medial **cell** proliferation three-fold seven days after **stenting** and virtually eliminated later intimal thickening. Six months after **stenting**, long after drug release and polymer degradation were likely complete, neointimal area was two-fold lower in **paclitaxel**-releasing **stents**. Tissue responses in **paclitaxel**-treated vessels included incomplete healing, few **smooth muscle cells**, late persistence of macrophages and dense fibrin with little collagen. CONCLUSIONS: Poly(lactide-co-sigma-caprolactone) copolymer-coated **stents** permit sustained **paclitaxel** delivery in a manner that virtually abolishes neointimal hyperplasia for months after **stent** implantation, long after likely completion of drug delivery and polymer degradation.
CT Check Tags: Animal; Support, U.S. Gov't, P.H.S.
*Angiogenesis Inhibitors: AD, administration & dosage
Coronary Disease: PA, pathology
*Coronary Disease: PC, prevention & control
*Drug Delivery Systems
***Paclitaxel: AD, administration & dosage**
Rabbits
Recurrence
***Stents**
Time Factors
Tunica Intima: DE, drug effects

*Tunica Intima: PA, pathology
RN **33069-62-4 (Paclitaxel)**
CN 0 (Angiogenesis Inhibitors)

L90 ANSWER 52 OF 55 MEDLINE on STN
AN 2000461063 MEDLINE
DN 20357889 PubMed ID: 10900668
TI [**Paclitaxel**: a chemotherapeutic agent for prevention of **restenosis**? Experimental studies in vitro and in vivo].
Paclitaxel: Ein Chemotherapeutikum zur **Restenoseprophylaxe**? Experimentelle Untersuchungen in vitro und in vivo.
AU Herdeg C; Oberhoff M; Siegel-Axel D I; Baumbach A; Blattner A; Kuttner A; Schroder S; Karsch K R
CS Medizinische Universitatsklinik III, Tubingen.. christian-herdeg@t-online.de
SO ZEITSCHRIFT FUR KARDIOLOGIE, (2000 May) 89 (5) 390-7.
Journal code: 0360430. ISSN: 0300-5860.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA German
FS Priority Journals
EM 200009
ED Entered STN: 20001005
Last Updated on STN: 20001005
Entered Medline: 20000926
AB **Paclitaxel**, a potent anti-tumor agent, shifts the cytoskeleton equilibrium towards assembly of altered and extraordinarily stable microtubules. These cellular modifications lead to reduced proliferation, **migration**, and signal transduction. It is highly lipophilic, which promotes a rapid cellular uptake, and has a long-lasting effect in the **cell** due to the structural alteration of the cytoskeleton. This makes **paclitaxel** a promising candidate for local drug delivery intended to address the proliferative and **migratory** processes involved in **restenosis**. In this article, results of our in vitro and in vivo studies with **paclitaxel** are presented. **Cell** culture experiments with monocultures of human arterial **smooth muscle cells** as well as co-cultures with human endothelial **cells** showed that **paclitaxel** leads to an almost complete growth inhibition within a dose range of 1.0-10.0 mumol/l, even after a short (20 min) single dose application. The comparison of an active, semi-active, and passive delivery system (porous balloon, microporous balloon, and double balloon) favored the double balloon for the following in vivo experiments. Tubulin staining and electron microscopy enabled visualization of **paclitaxel** -induced vessel wall alterations. In the rabbit model, locally delivered **paclitaxel** resulted in reduced neointima formation and enlargement in vessel size; in the pig model, however, after **stenting**, this inhibition was not significant. Both reduced proliferation and enlargement in vessel size contribute to a preservation of vessel shape and are likely to be caused by a structural alteration of the cytoskeleton, which is also supported by **vascular** contraction force experiments.
CT Check Tags: Animal; Human; In Vitro
*Angiogenesis Inhibitors: PD, pharmacology
***Angioplasty, Transluminal, Percutaneous Coronary: IS, instrumentation**
*Cell Division: DE, drug effects
Cell Movement: DE, drug effects
Cells, Cultured
*Coronary Vessels: DE, drug effects
Coronary Vessels: PA, pathology
Dose-Response Relationship, Drug

*Endothelium, Vascular: DE, drug effects
Endothelium, Vascular: PA, pathology
English Abstract
Equipment Design
***Paclitaxel: PD, pharmacology**
Rabbits
Recurrence
***Stents**
Swine
Vascular Patency: DE, drug effects
RN **33069-62-4 (Paclitaxel)**
CN 0 (Angiogenesis Inhibitors)

L90 ANSWER 53 OF 55 MEDLINE on STN
AN 2000114579 MEDLINE
DN 20114579 PubMed ID: 10651157
TI Visualization and comparison of drug effects after local **paclitaxel** delivery with different catheter types.
AU Herdeg C; Oberhoff M; Baumbach A; Blattner A; Kuttner A; Schroder S; Haase K K; Karsch K R
CS Dept. of Medicine, University of Tuebingen, Germany.. christian.herdeg@t-online.de
SO BASIC RESEARCH IN CARDIOLOGY, (1999 Dec) 94 (6) 454-63.
Journal code: 0360342. ISSN: 0300-8428.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200002
ED Entered STN: 20000229
Last Updated on STN: 20000229
Entered Medline: 20000211
AB BACKGROUND: The microtubule stabilizing compound **paclitaxel** has proved to have potent antiproliferative effects on smooth muscle cells both in vitro and in vivo. It induces cellular modifications that result in reduced proliferation, **migration** and signal transduction by shifting the cellular microtubule equilibrium towards assembly. We therefore reasoned that a visualization of the altered cytoskeleton could enable an evaluation of the drug effects following local drug delivery. METHODS AND RESULTS: 3 catheters - the porous balloon, the microporous balloon and the double balloon catheter - were chosen for this study representing the spectrum from passive to active, pressure-driven delivery. After the induction of a defined plaque in the right carotid arteries of 40 New Zealand rabbits by electrical stimulation, 32 animals underwent balloon dilatation and 8 animals served as pre-interventional control group with electrostimulation only. In 24 animals (n = 8 in each group) subsequent local **paclitaxel** delivery (10 micromol/L) was performed. 8 animals served as control with angioplasty only. Vessels were excised 1 week following intervention. Immunohistochemistry with antibodies against bromodeoxyuridine, alpha-actin, macrophages, von Willebrand factor and alpha-tubulin was performed. Cytoskeletal changes were analyzed by electron microscopy. Tubulin staining and electron microscopy revealed changes with distinct staining patterns for the different catheters. Specific catheter-induced injuries could be identified for the porous and double balloon catheter. Intimal proliferation, percentage of macrophages and extent of injury favor the double balloon catheter for local **paclitaxel** delivery. CONCLUSIONS: The alterations of the cytoskeleton induced by **paclitaxel** allowed for the detection of drug action by staining of tubulin and electron microscopy. This enables an evaluation of transfer, distribution and drug effects directly in the vasculature without marker substances. The double balloon catheter appears to be best suited for local **paclitaxel** therapy.

CT Check Tags: Animal; Comparative Study
*Antineoplastic Agents, Phytogenic: AD, administration & dosage
Carotid Artery Diseases: DT, drug therapy
Carotid Artery Diseases: PA, pathology
***Catheterization**
Cytoskeleton: DE, drug effects
Cytoskeleton: PA, pathology
*Drug Delivery Systems: IS, instrumentation
Immunohistochemistry
Muscle, Smooth, Vascular: DE, drug effects
Muscle, Smooth, Vascular: PA, pathology
***Paclitaxel: AD, administration & dosage**
Rabbits
RN **33069-62-4 (Paclitaxel)**
CN 0 (Antineoplastic Agents, Phytogenic)

L90 ANSWER 54 OF 55 MEDLINE on STN
AN 1999333351 MEDLINE
DN 99333351 PubMed ID: 10406693
TI Antiproliferative **stent** coatings: **Taxol** and related compounds.
AU Herdeg C; Oberhoff M; Karsch K R
CS Department of Medicine, University of Tubingen, Germany. christian.herdeg t-online.de.
SO SEMINARS IN INTERVENTIONAL CARDIOLOGY, (1998 Sep-Dec) 3 (3-4) 197-9. Ref: 26
Journal code: 9606070. ISSN: 1084-2764.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199908
ED Entered STN: 19990827
Last Updated on STN: 19990827
Entered Medline: 19990817
AB The implantation of **stents** can prevent vessels from post interventional elastic recoil and appears to limit adverse remodelling. In order to inhibit in-**stent restenosis**, an additional release of antiproliferative agents from the **stent** itself might lead to a synergistic reduction of lumen renarrowing. **Paclitaxel** (**Taxol**) is a microtubule-stabilizing agent with potent antiproliferative activity. Unlike other antimitotic agents of the colchicine type, it shifts the microtubule equilibrium towards assembly, leading to reduced proliferation, **migration** and signal transduction. Moreover, important biological processes, such as the activation of some protein kinases, are associated with microtubule depolymerization and are therefore inhibited by **paclitaxel**. Several experimental in vitro and in vivo studies using local **paclitaxel** delivery to inhibit proliferation and lumen renarrowing have been performed already--with very encouraging results.
CT Check Tags: Animal; Human
Cell Division: DE, drug effects
*Coated Materials, Biocompatible
Coronary Disease: TH, therapy
Cytoskeleton: DE, drug effects
*Drug Delivery Systems
Microtubules
Muscle, Smooth, Vascular: DE, drug effects
***Paclitaxel: AD, administration & dosage**
Paclitaxel: PD, pharmacology
Paclitaxel: TU, therapeutic use

*Platelet Aggregation Inhibitors: AD, administration & dosage
Platelet Aggregation Inhibitors: PD, pharmacology
Platelet Aggregation Inhibitors: TU, therapeutic use
Prosthesis Design
Recurrence: PC, prevention & control
***Stents**
RN **33069-62-4 (Paclitaxel)**
CN 0 (Coated Materials, Biocompatible); 0 (Platelet Aggregation Inhibitors)

L90 ANSWER 55 OF 55 MEDLINE on STN
AN 95221643 MEDLINE
DN 95221643 PubMed ID: 7706494
TI **Taxol** inhibits neointimal smooth muscle cell accumulation after angioplasty in the rat.
AU Sollott S J; Cheng L; Pauly R R; Jenkins G M; Monticone R E; Kuzuya M; Froehlich J P; Crow M T; Lakatta E G; Rowinsky E K; +
CS Laboratory of Cardiovascular Science, National Institute on Aging, National Institutes of Health, Baltimore, Maryland 21224, USA.
SO JOURNAL OF CLINICAL INVESTIGATION, (1995 Apr) 95 (4) 1869-76.
Journal code: 7802877. ISSN: 0021-9738.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199505
ED Entered STN: 19950518
Last Updated on STN: 20020212
Entered Medline: 19950509
AB Despite significant improvements in the primary success rate of the medical and surgical treatments for atherosclerotic disease, including angioplasty, bypass grafting, and endarterectomy, secondary failure due to late **restenosis** continues to occur in 30-50% of individuals. **Restenosis** and the later stages in atherosclerotic lesions are due to a complex series of fibroproliferative responses to **vascular** injury involving potent growth-regulatory molecules (such as platelet-derived growth factor and basic fibroblast growth factor) and resulting in **vascular smooth muscle cell** (VSMC) proliferation, **migration**, and neointimal accumulation. We show here, based on experiments with both **taxol** and deuterium oxide, that microtubules are necessary for VSMCs to undergo the multiple transformations contributing to the development of the neointimal fibroproliferative lesion. **Taxol** was found to interfere both with platelet-derived growth factor-stimulated VSMC **migration** and with VSMC **migration** and with VSMC proliferation, at nanomolar levels in vitro. In vivo, **taxol** prevented medial VSMC proliferation and the neointimal VSMC accumulation in the rat carotid artery after balloon dilatation and endothelial denudation injury. This effect occurred at plasma levels approximately two orders of magnitude lower than that used clinically to treat human malignancy (peak levels achieved in this model were approximately 50-60 nM). **Taxol** may therefore be of therapeutic value in preventing human **restenosis** with minimal toxicity.
CT Check Tags: Animal
***Angioplasty, Balloon: AE, adverse effects**
*Carotid Arteries: DE, drug effects
Carotid Arteries: GD, growth & development
Carotid Arteries: PA, pathology
Carotid Arteries: SU, surgery
Cell Communication: DE, drug effects
Cell Division: DE, drug effects
Cell Movement: DE, drug effects
Cells, Cultured
Deuterium Oxide: PD, pharmacology

Dose-Response Relationship, Drug
Immunohistochemistry
Microtubules: DE, drug effects
Muscle Development
***Muscle, Smooth, Vascular: DE, drug effects**
Muscle, Smooth, Vascular: GD, growth & development
Muscle, Smooth, Vascular: PA, pathology
***Paclitaxel: PD, pharmacology**
Platelet-Derived Growth Factor: PD, pharmacology
Rats
Rats, Wistar
*Tunica Intima: DE, drug effects
Tunica Intima: GD, growth & development
Tunica Intima: PA, pathology
RN **33069-62-4 (Paclitaxel)**; 7789-20-0 (Deuterium Oxide)
CN 0 (Platelet-Derived Growth Factor)

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FILE 'WPIX' ENTERED AT 10:33:15 ON 20 JAN 2004
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FILE LAST UPDATED: 15 JAN 2004 <20040115/UP>
MOST RECENT DERWENT UPDATE: 200404 <200404/DW>
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/BIX is also provided which comprises both /BI and /ABEX <<<

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DERWENT UPDATE 200403.
THE TIME RANGE CODE WILL ALSO CHANGE FROM 018 TO 2004.
SDIS USING THE TIME RANGE CODE WILL NEED TO BE UPDATED.
FOR FURTHER DETAILS: http://thomsonderwent.com/chem/polymers/ <<<

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L122 ANSWER 1 OF 16 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2004-042413 [04] WPIX
DNN N2004-034283 DNC C2004-017342
TI New aminated oligo- or polysaccharide derivatives obtained from heparin, chitosan or chitin, useful for producing hemocompatible coatings on medicinal products, especially **stents**.
DC A11 A18 A28 A89 A96 B05 B07 D22 J01 P34
IN FAUST, V; HOFFMANN, M; HORRES, R; LINSSEN, M K; DI BIASE, D; HOFFMANN, E

PA (HEMO-N) HEMOTEQ GMBH
CYC 103
PI WO 2003094990 A1 20031120 (200404)* DE 93p A61L031-16
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
DE 10221055 A1 20031127 (200404) C08B037-08
ADT WO 2003094990 A1 WO 2003-DE1253 20030415; DE 10221055 A1 DE 2002-10221055 20020510
PRAI DE 2002-10221055 20020510; US 2002-378676P 20020509
IC ICM A61L031-16; C08B037-08
ICS A61L033-08; C08B037-10; C08L005-10
AB WO2003094990 A UPAB: 20040115
NOVELTY - Aminated oligo- or polysaccharide derivatives (I), containing N-acyl-glucosamine or N-acyl-galactosamine units and obtained by modification of heparin, chitosan or chitin, are new.

DETAILED DESCRIPTION - Aminated oligo- or polysaccharide derivatives (I) of formula (IA) or (IB) and their salts are new.

n = 4-1050;

X, Y = CHO, COCH3, COC2H5, COC3H7, COC4H9, COC5H11, COCH(CH3)2, COCH2CH(CH3)2, COCH(CH3)C2H5, COC(CH3)3, CH2COO-, C2H4COO-, C3H6COO- or C4H8COO-.

INDEPENDENT CLAIMS are included for:

(a) the preparation of (I);

(b) (I) obtained by the process (b);

(c) the use of (I) in the production of hemo-compatible coatings on medicinal products;

(d) the use of oligo- and/or polysaccharides (II) for hemo-compatible coating of surfaces, where 40-60% of the sugar units of (II) are N-acyl-glucosamine or N-acyl-galactosamine and the remaining sugar units contain one carboxy group per unit (specifically being uronic acids, especially D-glucuronic acid and L-iduronic acid);

(e) a hemo-compatible coating method for biological and/or artificial surfaces of medicinal products, involving applying a hemocompatible layer of (I) or (II) to the surface and/or applying a biostable layer on the surface of the product or the hemo-compatible layer; and

(f) medicinal products obtained by the process (e).

ACTIVITY - Anticoagulant; Vasotropic.

MECHANISM OF ACTION - None given in the source material.

USE - The use of (I) or (II) is claimed in the production of hemo-compatible coatings on medicinal products, specifically by covalent bonding to the products. The claimed medicinal products are specifically **prostheses**, organs, blood vessels, aortas, heart valves, tubes, artificial organ parts, **implants**, fibers, hollow fibers, **stents**, canulas, syringes, membranes, preserves, blood containers, titer plates, cardiac pacemakers, adsorbent media, chromatographic media or columns, dialyzers, connectors, sensors, valves, centrifuge chambers, heat exchangers, endoscopes, filters or pump chambering pieces; the use of such products is claimed for direct contact with blood and for inhibiting or reducing protein adhesion to the surfaces, especially for inhibiting or reducing non-specific protein deposition on titer plates (or other carrier media for diagnostic tests), adsorber media or chromatographic media. The products are especially **stents** (optionally having a coating layer containing 0.001-10 mg/cm2 of antiproliferative, antiinflammatory and/or antithrombotic agent (III')); the use of such **stents** is claimed for inhibiting or reducing **restenosis** and/or for continuous release of (III').

ADVANTAGE - (I) provide hemo-compatible, biocompatible, athrombogenic coatings which cause no undesirable reactions or side-effects even on

long-term use.
Dwg.0/18
FS CPI GMPI
FA AB; GI; DCN
MC CPI: A12-L04; **A12-V02**; A12-V03; B01-A02; B04-C01C; B04-C01F; B04-C02; B04-C03; B04-H19; B04-N02; B04-N04A; B06-D09; B06-E05; B07-A02B; B08-D01; B10-C02; B10-D01; B11-C09; **B14-F01G**; B14-F04; B14-H01B; **D09-C01**; J01-H
TECH UPTX: 20040115
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: Claimed preparation of (IA) involves completely desulfating heparan sulfate or heparan sulfate-heparin with acid, the N-acylating. Claimed preparation of (B) involves partially N-carboxyalkylating chitosan then N-acylating; partially N-acylating chitosan then N-carboxyalkylating; or partially deacetylating chitin then carboxyalkylating. Preferably approximately half of the amino groups of chitin or chitosan are acylated and the other half are N-carboxyalkylated. Preferably the products contain less than 0.05 sulfate groups per disaccharide unit and less than 1% free amino groups based on the total -NHY groups.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: The coating of medicinal products optionally further includes application of a biodegradable and/or biostable layer containing covalently and/or adhesively bonded active agent(s) (III), by dipping or spraying, over the hemocompatible or biostable layer; or incorporating (III) in the hemocompatible or biostable layer. The hemocompatible layer may be of derivatives of native heparin (prepared regio-selectively, in the molecular weight region from pentasaccharide to 13 kD and having various sulfation and acylation), heparan sufate (or derivatives), oligo- or polysaccharides of the erythrocyte glycocalix, desulfated and reacylated heparin and/or N-carboxymethylated and/or partially N-deacylated chitosan. Numerous (about 450) preferred active agents (III) are specified in the claims, e.g. tacrolimus, thymosin alpha-1, **paclitaxel**, trapidil, alpha- or beta-estradiol, simvastatin, macrocyclic carbon suboxide, colchicine, fumaric acid or melanocyte stimulating hormone.

TECHNOLOGY FOCUS - POLYMERS - Preferred Materials: About 100 preferred biodegradable coating materials are specified in the claims, e.g. polyvalerolactone, polylactide, polyhydroxybutyrate, poly-p-dioxanone, fibrin, polycyanoacrylate, polyorthoester, polyvinyl pyrrolidone, polyvinyl alcohol, polyphosphazene, flexible polyurethane, starch, collagen, polyaminoacid, chitosan, heparin, dextran or gum arabic. About 75 preferred biostable coating materials are specified in the claims, e.g. polyacrylic acid, polymethyl methacrylate, polyacrylonitrile, polyamide, polycarbonate, polyvinyl halide, polyethylene, PTFE, silicone-polyurethane, polyethylene terephthalate, cellulose acetate, epoxy resin, plydimethyl siloxane or chitosan.
ABEX UPTX: 20040115
EXAMPLE - A solution of 1 g sodium heparin in 10 ml water was supplied to a column of 100 ml Amberlite IR-122 (RTM; cation exchange resin; previously converted into the H+ form), followed by elution with 400 ml water. The eluate was dripped into a vessel containing 0.7 ml pyridine and adjusted to pH 6 with pyridine, followed by lyophilization. A mixture of 0.9 g of the obtained heparin-pyridinium salt (0.9 g) and 90 ml of 6/3/1 (by volume) mixture of dimethyl sulfoxide, 1,4-dioxan and methanol was heated at 90degreesC for 24 hours, treated with 823 mg pyridinium chloride, heated at 90degreesC for 70 hours, diluted with 100 ml water, adjusted to pH 9 with sodium hydroxide, dialyzed against water and lyophilized. A solution of 100 mg of the obtained desulfated heparin in 10 ml water was treated successively at 0degreesC under stirring with 1.5 ml methanol, 4 ml Dowex 1-4 (RTM; anion exchange resin; in OH- form) and 150 microl acetic anhydride, stirred for 2 hours at 4degreesC, filtered, dialyzed against water and lyophilized to give desulfated, re-acetylated

heparin.

DEFINITIONS - Preferred Definitions:
X, Y = COCH3, COC2H5, COC3H7, CH2COO-, C2H4COO- or C3H6COO- in (IA); and
Y = COCH3, COC2H5 or COC3H7 in (IB).

L122 ANSWER 2 OF 16 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-480259 [45] WPIX
CR 2002-009996 [01]; 2002-049493 [06]; 2002-055636 [07]; 2002-055643 [07]; 2002-055644 [07]; 2002-089834 [12]; 2002-154437 [20]; 2002-179028 [23]; 2002-537167 [57]
DNN N2003-381782 DNC C2003-128383
TI Medical device for treatment of vascular diseases comprises scaffold structure for maintaining luminal patency, biocompatible vehicle affixed to portion of scaffold structure, and agent(s) in therapeutic dosages.
DC B07 D22 P32 P34
IN FALOTICO, R; SPALTRO, J
PA (CRDC) CORDIS CORP; (FALO-I) FALOTICO R; (SPAL-I) SPALTRO J
CYC 33
PI US 2003060877 A1 20030327 (200345)* 47p A61F002-06
EP 1362602 A1 20031119 (200377) EN A61L031-10
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR
CA 2425696 A1 20031015 (200379) EN A61F002-06
ADT US 2003060877 A1 CIP of US 2001-962496 20010925, US 2002-122978 20020415; EP 1362602 A1 EP 2003-252350 20030414; CA 2425696 A1 CA 2003-2425696 20030414
PRAI US 2002-122978 20020415; US 2001-962496 20010925
IC ICM A61F002-06; A61L031-10
ICS A61B017-22; A61L029-08; A61L029-16; A61L031-16; **A61M025-10**; **A61M037-00**; A61P007-00; **A61P009-00**; **A61P009-10**
AB US2003060877 A UPAB: 20031208
NOVELTY - A medical device comprises scaffold structure for maintaining luminal patency, biocompatible vehicle affixed to portion of scaffold structure, and agent(s) in therapeutic dosages incorporated into the biocompatible vehicle. The biocompatible vehicle is configured to release agent(s) over time period(s) to treat both acute phase and chronic phase of vascular disease.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a method for treating atherosclerotic vulnerable plaque comprising maintaining vessel patency and providing structural support for fibrous cap of the vulnerable plaque lesion through the introduction of coated **stent**; releasing first agent(s) in therapeutic dosage incorporated into coated **stent** at first rate and first duration; and releasing second agent in therapeutic dosage incorporated into coated **stent** at second rate and second duration.

ACTIVITY - Vasotropic; Antiarteriosclerotic.
No biological data is given.
MECHANISM OF ACTION - None given.

USE - For treatment of acute phase and chronic phase of vascular disease, e.g. atherosclerotic vulnerable plaque (claimed).

ADVANTAGE - The invention minimizes or eliminates biological organism's reaction to the introduction of device to organism.

DESCRIPTION OF DRAWING(S) - The figure is a cross-sectional view of a band of the **stent** having drug coatings.

Dwg.7/27
FS CPI GMPI
FA AB; GI; DCN
MC CPI: B01-B02; B04-C03; B06-A03; B06-E05; B11-C04A; **B12-M10A**; B14-C03; B14-D05D; B14-D06; B14-D07C; B14-F02; B14-F04; B14-F06; B14-F07; B14-H01B; B14-H04; B14-L01; B14-L06; D09-C01D
TECH UPTX: 20030716

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Component: The scaffold structure comprises **stent**. The **stent** is balloon expandable or self-expanding. The biocompatible comprises polymeric coating having layer(s) configured to release agent(s) at first rate and for first duration to treat the acute phase of the vascular disease, and to release agent(s) at second rate and for second duration to treat chronic phase of vascular disease.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Component: The agent(s) comprises lipid-lowering agent incorporated into layer(s). The lipid lowering agent comprises an 3-hydroxy-3-methylglutaryl (HMG) co-enzyme reductase inhibitor or statin, antiinflammatory/inflammation blocking agent, antiproliferative, antithrombogenic, rapamycin, dexamethasone, antiinflammatory corticosteroids, rapamycin derivatives, rapamycin analogs, direct inhibitor of the target of rapamycin kinase (mTOR), taxane including **paclitaxel** and taxane derivatives that inhibits microtubule function, cyclin dependent kinase inhibitor that will block the cell cycle, retinoid, growth factor receptor kinase inhibitor, farnesyl transferase inhibitor, P38 MAP kinase inhibitor, antagonist of tumor necrosis factor, mast cell stabilizer, protease inhibitor including matrix metallo-protease inhibitor, antiapoptotic agent, transforming growth factor (TGF) beta agonist, and vitronectin antagonist.

L122 ANSWER 3 OF 16 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2003-403063 [38] WPIX
CR 2003-468179 [44]
DNC C2003-107283
TI Composition used for controlled release of drugs e.g. oligonucleotide therapeutics comprises hydroxyapatite complexed with agent and polymeric carrier.
DC B05 B07
IN BURT, H M; JACKSON, J; SPRINGATE, C; WONG, W; JACKSON, J K
PA (BURT-I) BURT H M; (JACK-I) JACKSON J; (SPRI-I) SPRINGATE C; (WONG-I) WONG W; (ARCP-N) ARC PHARM INC; (UYBR-N) UNIV BRITISH COLUMBIA
CYC 101
PI WO 2003030943 A1 20030417 (200338)* EN 31p A61K047-48
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
US 2003134811 A1 20030717 (200348) A61K048-00
ADT WO 2003030943 A1 WO 2002-CA1514 20021008; US 2003134811 A1 Provisional US 2001-328175P 20011009, Provisional US 2001-328379P 20011009, US 2002-259277 20020926
PRAI US 2001-328379P 20011009; US 2001-328175P 20011009; US 2002-259277 20020926
IC ICM A61K047-48; A61K048-00
ICS A61K031-337; A61K031-525; A61K047-02
AB WO2003030943 A UPAB: 20030729
NOVELTY - Composition (C1) comprises at least one hydroxyapatite (HAP) complexed with at least one agent (a1) to form at least one microparticulate compartment for controllably releasing (a1). The compartment is complexed with at least one polymeric carrier which also modulates the release of (a1).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) a composition (C2) which comprises HAP complexed with at least one oligonucleotide therapeutic (b1) having less than 100 nucleotides, and additionally comprising at least one of an adjuvant, excipient, buffer and a diluent;

(2) a surgical device comprising (C1) or (C2), and

(3) a kit comprising (C1), (C2) or the surgical device in a container (preferably a syringe or vial).

ACTIVITY - Cytostatic; Antiarthritic; Antipsoriatic; Antiinflammatory; Vasotropic; Immunosuppressive; Neuroprotective; Antiarteriosclerotic; Antibacterial.

In a test, tumor growth inhibition by clusterin antisense oligonucleotide (clusterin ASO) was evaluated on PC-3 human prostate tumors in SCID mice by administering a composition (100 mg) comprising (in weight/weight%) hydroxyapatite (6), clusterin antisense oligonucleotide (clusterin ASO) microparticulate (2) and docetaxol (1). The results showed that the composition inhibited tumor growth for 5 weeks indicating controlled release of docetaxol and clusterin ASO with prolonged effectiveness of the drugs.

MECHANISM OF ACTION - None given.

USE - Used for the controlled release of drugs, in surgical devices e.g. **stent** (including esophageal, gastrointestinal, vascular, biliary, colonic, pancreatic, ureteric, urethral, lacrimal, eustachian tube, fallopian tube, nasal, sinus, tracheal and bronchial **stent**), **catheter**, port, shunt, device for continuous subarachnoid infusion, feeding tube, solid **implant** to prevent surgical adhesion, uterine **implant**, artificial sphincter, periurethral **implant**, splint, ophthalmic **implant**, contact lens, and plastic surgery **implant** for **implantation** into patients and for treating proliferative and inflammatory diseases e.g. cancer, arthritis, psoriasis, and surgical adhesion in humans (all claimed). The compositions are also used for treating **restenosis**, graft rejection, inflammatory bowel disease, multiple sclerosis, inflammatory lung disease, atherosclerosis, vasospasms, autoimmune conditions, and infectious diseases.

ADVANTAGE - (C1) Controllably modulates the release of chemotherapeutic levels of additional agents. The composition protects (a1) from degradative processes, maintains either locally or systemically the concentration of (a1) through controlled release, avoids the classic peaks and troughs of plasma drug concentrations observed when rapidly cleared drugs are repeatedly administered to the systemic circulation, reduces the frequency and amount of administration of (a1) or other drugs, reduces the toxicities or side effects due to (a1) or other drugs in the body, reduces the elimination of the drugs or (a1) from the body and reduces the need for vectoring agents as the diffusion of the antisense agents into the target cells can be achieved by maintaining the product concentrations. The composition also improves the efficiency or reduces the toxicity of additional agents.

Dwg.0/1

FS CPI

FA AB; DCN

MC CPI: B04-B03C; B04-E07; B04-L01; B05-A01B; B05-B02A3; B06-A03; B06-D09; B12-M11D; B12-M11E; B14-C07; B14-C08; B14-F02B; B14-F02C; B14-F02D; B14-F09; B14-G02A; B14-J01B2; B14-K01A; B14-K01B; B14-L09

TECH UPTX: 20030616

TECHNOLOGY FOCUS - BIOLOGY - Preferred Components: (a1) Comprises an oligonucleotide therapeutic (preferably anionic) comprising at least one of a ribozyme and an antisense oligonucleotide. (b1) Comprises at least one of a ribozyme, an antisense oligonucleotide and an immune modulating oligonucleotide.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: (C1) Also comprises at least one agent (a2), at least one phosphate ion source and optionally a cell permeation enhancing agent. The phosphate ion source provides a mildly alkaline local environment relative to an in vivo environment. (C2) Comprises a paste.

(C1) Is a film having a thickness of less than 2 mm and a tensile strength of greater than 70 N/cm2. (C1) releases (a1) (greater than 10 wt./wt.%)

for 5-15 (preferably at least 15) days.
Preferred Components: (a2) Comprises at least one of an antiproliferative drug, antiinflammatory drug, antidiabetic, antimicrobial, anesthetic, vasoconstrictor, vasodilator, cardiotonic, enzyme, hormone, bone metabolism controlling agent, hypotensive, sedative, anticancer agent, antihistamine, antitussive, vaccine or asthma treatment drug (preferably **paclitaxel** or methotrexate).
Preferred Kit: The kit also comprises a notice associated with the container and instructions about at least one of use of (C1) or (C2), dosing and mode of administration. The notice is in a form prescribed by a governing agency regulating (C1) or (C2).

TECHNOLOGY FOCUS - MECHANICAL ENGINEERING - Preferred Device: The device is a venous access device comprising an external tunneled **catheter** , **implanted** port, epidural **catheter** or central **catheter** (PICC).

TECHNOLOGY FOCUS - POLYMERS - Preferred Components: The HAP comprises porous microparticles. The polymeric carrier is a paste encapsulating the microparticulate compartment. The microparticulate compartment is micronized.

ABEX UPTX: 20030616
ADMINISTRATION - The dosage is 5-2000 (especially 60-500) mg/m2 orally, nasally, rectally, intravenously, intraperitoneally, intramuscularly, subcutaneously, topically, intraarticularly, by injection through a syringe needle, intratumorally or by **implanting** a device (claimed). (C1) Is administered in the form of an ointment, cream, capsule, lotion, gel, spray, foam, mousse, coating, wrap, barrier, **implant**, microsphere or film.

EXAMPLE - A composition comprising hydroxyapatite (HAP) and clusterin antisense oligonucleotide (clusterin ASO) was prepared by forming microparticulate from a solution of HAP (74 mg) and clusterin ASO (36 mg) in water (500 micro-l). Methoxypolyethylene glycol 350 (600 mg) and a waxy polymer (400 mg) were heated at 40degreesC in a ratio of 60:40 to form a polymeric paste. HAP/clusterin ASO microparticulate (40 mg) was added to the paste (1000 mg) and heated at 40degreesC for 15 minutes to form a controlled release composition.

L122 ANSWER 4 OF 16 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-750514 [81] WPIX
DNN N2002-591081 DNC C2002-212685
TI Medical **stent** useful for treatment of stenosed vasculature or other body passages having a coating comprising a primer layer comprising a first composition and drug reservoir layer comprising second composition.
DC A96 B05 B07 D16 D22 P32
IN CALISTRI-YEH, M; CHAMBERLAIN, A M; HULLIHEN, D G; ROSEBROUGH, S F; WHITBOURNE, R J
PA (STSB-N) STS BIOPOLYMERS INC
CYC 100
PI WO 2002074194 A2 20020926 (200281)* EN 45p A61F000-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
ADT WO 2002074194 A2 WO 2002-US8039 20020318
PRAI US 2001-276089P 20010316
IC ICM A61F000-00
AB WO 200274194 A UPAB: 20021216

NOVELTY - Medicated **stent** (S1) with a coating comprising a primer layer (a) comprising a first composition (a1) of at least one polymer, and a drug reservoir layer (b) comprising a second composition (b1) of at least one polymer and active agent(s). The coating remains intact upon **stent** expansion and releases drug at site of expansion.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) Preparation of the medicated **stent** (S1) by

(1) either applying a primer polymer liquid comprising at least one polymer in a volatile medium, applying a drug reservoir polymer liquid comprising at least one polymer in a volatile medium, applying an active agent either together with or after applying the drug reservoir polymer liquid and removing the volatile media; or

(2) applying (a) and (b) comprising at least two polymers and at least one active agent; and

(2) Administration of a bioactive agent to a target site in a subject involving **implanting** S1 at the target site of the subject and expanding to allow active agent to elute from the coating during an extended period;

ACTIVITY - Vasotropic; Anticoagulant; Thrombolytic.

MECHANISM OF ACTION - None given in source document.

USE - For administering a bioactive agent to a target site in a subject (claimed) and for the treatment of stenosed vasculature or other body passages.

ADVANTAGE - The **stent** provides therapeutic activity from the surfaces of **stents** in order to reduce the incidence of **restenosis** and thrombus formation after coronary **stenting** procedures in the clinic. The polymer layers possess excellent flexibility and elasticity and are expandable. The polymers are not bioerodable such that differences in hormonal activity from patient to patient are minimized. The polymer layer provides reservoirs for a variety of drugs or drug cocktails.

Dwg.0/1

FS CPI GMPI

FA AB; DCN

MC CPI: A11-B05D; A12-V03D; B01-B02; B04-B03C; B04-B04D2; B04-C01; B04-C03; B04-E01; B04-G21; B04-H06; B04-L01; B04-N04; B04-N06; B05-A03B; B05-B02C; B05-C07; B06-H; B07-H; B10-B02J; B10-C04C; B10-E02; **B11-C04B**; **B12-M10**; B14-D03; B14-F01; **B14-F01G**; B14-F02; B14-F04; B14-L06; D05-C01; D05-C02; D05-C03; D05-C11; D05-H10; D05-H11A; D05-H12A; **D09-C01B**

TECH UPTX: 20021216

TECHNOLOGY FOCUS - POLYMERS - Preferred **Stent**: (S1) further comprises an intermediate layer between (a) and (b), and at least one image enhancing material in one of the layers or in a separate layers that is capable of enhancing visibility in ultra sound, magnetic resonance imaging or X ray imaging. The different agents contained within the same and/or different layers. The coating of S1 has a thickness of 0.3 - 30 microm.

Preferred Layer: (a) and/or (b) is a single layer (preferably at least two layers). The intermediate layer comprises multiple layers. (a) comprises polymers selected from acrylate polymer/copolymer, acrylate carboxyl and/or hydroxyl copolymer, polyvinylpyrrolidone/vinylacetate copolymer (PVP/VA), olefin acrylic acid copolymer, ethylene acrylic acid copolymer, epoxy polymer, polyethylene glycol, polyethylene oxide, polyvinylpyridine copolymers, polyamide polymers/copolymers polyimide polymers/copolymers, polyether sulfones, polyurethane, polycarbonate urethane polymer, and/or silicone urethane polymer (preferably at least one acrylate/carboxyl polymer, epoxy polymer, or polyvinylpyrrolidone vinylacetate copolymer (PVP/VA), especially at least one ethylene acrylic acid copolymer (EAA), epoxy polymer, or polycarbonate urethane). The intermediate layer comprises at least one polymer selected from acrylate polymer/copolymer,

acrylate carboxyl and/or hydroxyl, PVP/VA, polyurethane, silicone urethane polymer, polycarbonate urethane polymer, polyvinylbutyral, and/or epoxy polymers (preferably polyurethane, polycarbonate urethane polymer, or silicone urethane polymer, especially polycarbonate polyurethane). (b) is selected from acrylate polymer/copolymer, acrylate hydroxyl and/or carboxyl copolymer, polyvinyl pyrrolidone (PVP), PVP/VA, cellulose - ester, polyurethane, polycarbonate-urethane polymer, silicone-urethane polymer, epoxy polymer, polyethylene glycol and/or polyethylene oxide (preferably acrylate polymer/copolymer, acrylate polymer/copolymer containing carboxyl and/or hydroxyl groups, cellulose nitrate and/or other cellulose ester, especially polyurethane, polycarbonate urethane polymer, or silicone urethane polymer, particularly at least one polyurethane, cellulose nitrate, and/or at least one other cellulose ester polymer). The polymers have flexural modulus greater that 1000 psi and elongation at break greater than 200%. (a) has a thickness of 0.1-5 microm. (b) has a thickness of 0.1-10 microm. The intermediate layer has a thickness of 0.1-15 microm. The drug releasing layer comprises at least one acrylate/carboxyl polymer, epoxy polymer or polyvinylpyrrolidone vinylacetate copolymer (PVP/VA) (preferably at least one polytetramethylene ether glycol urethane, polycarbonateurethane, silicone-urethane polymer, polyethylene glycol, polymethylmethacrylate-2-hydroxyethylethacrylate copolymer, polyethylmethacrylate-2-hydroxyethylmethacrylate copolymer, polypropylmethacrylate-2-hydroxyethylmethacrylate copolymer, polybutylmethacrylate-2-hydroxyethylmethacrylate copolymer, polymethylacrylate-2-hydroxyethylmethacrylate copolymer, polyethylacrylate-2-hydroxyethylmethacrylate copolymer, polypropylacrylate-2-hydroxymethacrylate copolymer, polybutylacrylate-2-hydroxyethylmethacrylate copolymer, copolymermethylvinylether maleicanhydride copolymer or poly(2-hydroxyethyl methacrylate, especially nitrocellulose).

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: The active agent comprises an anti-restenotic agent effective at a **stented** site. The active agent is selected from at least one anti-thrombogenic agent, anti-inflammatory agent, antineoplastic agent, anti-proliferative agent, cytostatic agent, cytotoxic agent, antimicrobial agent, anti-restenotic agent, anti-platelet agent, or anti-coagulant agent (preferably anti-fibrin and fibrinolytic agent, anti-platelet agent, prostacyclin and its analogues, glycoprotein IIb/IIIa agent, thromboxane inhibitor, anti-thrombin and anticoagulant agent, anti-mitotic, antiproliferative and cytostatic agent, antiangiogenic and angiostatic agent, ACE inhibitor, growth factor antagonist, antioxidant, vitamin, calcium channel blocker, fish oil (omega 3-fatty acid), phosphodiesterase inhibitor, nitric acid donor, somatostatin analogue, immunosuppressive and antiinflammatory agent, antimicrobial, radionuclide including alpha, beta and gamma emitting isotope, COX-2 inhibitor, endothelial promoter, kinase inhibitor, epidermal growth factor kinase inhibitor, tyrosine kinase inhibitor, MAP kinase inhibitor, and protein transferase inhibitor, especially plasmin, streptokinase, single chain urokinase, urokinase, t-PA (tissue type plasminogen activator), aminocaproic acid, aspirin, monoclonal antibody, peptide, reopro, Cilastagel, eptifibatide, tirofiban, ticlopidine, Vapiprost, dipyridamole, forskolin, angiopeptin, argatroban, dextan, heparin, LMW heparin, enoxaparin, dalteparin, hirudin, recombinant hirudin, anti-thrombin, synthetic antithrombin, thrombin inhibitor, warfarin, other coumarin, vincristine, vinblastine, **paclitaxel** and its analogue, methotrexate, cisplatin, fluorouracil, rapamycin, azathioprine, cyclophosphamide, mycophenolic acid, corticosteroid, colchicine, nitroprusside, **paclitaxel**, angiostatin and endostatin; genetic material, oligonucleotide, cilazapril, lisinopril, captopril, VEGF, FGF, probucol, tocopherol, nifedipine, dipyridamole, molsidomine, angiopeptin, prednisolone, glucocorticoid, dexamethasone, rifamycin, Re-188, Re-186, I-125, Y-90 celecoxib, Vioxx, dipyridamole or theophylline, especially **paclitaxel**, heparin complex, rifamycin

or methotrexate).
Preferred Method: The method involves applying more than one active agent. The method further involves applying an intermediate flexibilizing polymer liquid comprising at least one polymer that differs from (a) and (b). The volatile media has a boiling point of greater that 110degreesC. The liquid has a viscosity of 20-70 cps.

ABEX UPTX: 20021216
EXAMPLE - A hybrid polymer bonding layer solution (containing polyurethane 1 (%) (0.78), ethylene acrylic acid copolymer (EAA) (3.05), epoxy (0.90), dimethyl acetamide (DMAC) (2.67), cyclohexanone (33.66), tetrahydrofuran (THF) (58.94)) was applied and dried at 120degreesC for 60 minutes. An intermediate layer (containing polyurethane 1 (%) (8.80), DMAC (66.20), cyclohexanone (25)) was applied and dried at 120degreesC for 60 minutes. The drug release hybrid polymer layer (containing polyurethane 2 (%) (6.07), cellulose ester 1 (2.43), THF (54.64), ethanol (21.85), dimethylsulfoxide (DMSO) (15.01)) was applied and dried at 75degreesC for 60 minutes. A high boiling point solvent was included in each formulation to aid in processing. Drug(s) was imbibed into the drug release hybrid polymer layer. **Stent** samples were coated with these layers had good uniformity based on dye testing. The coated **stents** were found to be expandable proved quite flexible and demonstrated excellent adhesion to the substrate.

L122 ANSWER 5 OF 16 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-740703 [80] WPIX
DNN N2002-583608 DNC C2002-209680
TI Drug eluting endovascular device for delivering locally therapeutic agents within adjacent tissues comprises an endovascular device, a hydrophobic linker molecule, and a lipophilic drug passively deposited on the linker molecule.
DC B05 B07 D22 M11 P32 P34 P42
IN BOURGUIGNON, B; LAWRENCE, M F; LECLERC, G; LEVESQUE, L
PA (BOUR-I) BOURGUIGNON B; (LAWR-I) LAWRENCE M F; (LECL-I) LECLERC G; (LEVE-I) LEVESQUE L; (ANGI-N) ANGIOGENE INC
CYC 100
PI WO 2002066092 A2 20020829 (200280)* EN 41p A61L031-16
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
US 2002119178 A1 20020829 (200280) B05D003-00
ADT WO 2002066092 A2 WO 2002-CA231 20020222; US 2002119178 A1 Provisional US 2001-270605P 20010223, US 2002-80499 20020222
PRAI US 2001-270605P 20010223; US 2002-80499 20020222
IC ICM A61L031-16; B05D003-00
ICS A61F002-00
AB WO 200266092 A UPAB: 20021212
NOVELTY - A drug eluting endovascular device comprises an endovascular device (i), a hydrophobic linker molecule (ii) containing a diazonium moiety electrodeposited onto the surface of (i), and a lipophilic drug (iii) passively deposited on (ii) and bound to (ii) through hydrophobic interactions which will elute over time from (i).
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for loading a drug onto an endovascular device involving:
(1) electroplating (ii) onto the surface of (i) to obtain a functionalized surface of the device; and
(2) depositing passively (iii) onto the functionalized surface.
The drug binding to the diazonium moiety of (ii) slowly elutes into a tissue when the device is brought in contact with the tissue in vivo.
ACTIVITY - Vasotropic.

No suitable biological data given.

MECHANISM OF ACTION - None given in source material.

USE - The drug eluting endovascular device is used for the treatment of a vascular disease e.g. **restenosis**, arteriovenous malformation, arteriovenous fistulae, hypervascular lesion, neoplastic lesion and asymptomatic carotid carvenous fistulae (all claimed) and for delivering locally therapeutic agents within the adjacent tissues such as an arterial wall for treating vascular diseases.

ADVANTAGE - The lipophilic properties of the therapeutic agents hold them on the **stent** and allow their sustained release. Following the deposition treatment, no adverse effects are observed in coated **stent** in vitro (mechanical properties) and in vivo (clotting thrombogenicity). As the active component is delivered directly to the appropriate region the efficacy of drug transfer is greatly increased.

Dwg.0/10

FS CPI GMPI

FA AB; DCN

MC CPI: B01-B01; B02-A; B02-B; B02-R; B04-C02E1; B06-H; B07-H; B10-A05; B10-A15; B10-B01A; B10-B03B; B10-B04B; B10-C04B; B11-C03; B11-C04A; **B12-M10A**; **B14-F01G**; B14-F02; B14-H01B; **D09-C01B**; M11-B

TECH UPTX: 20021212

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Device: The endovascular device is made of stainless steel.

Preferred Drug: (iii) is selected from:

(1) anti-proliferative agent;

(2) anti-inflammatory agent;

(3) anti-thrombotic drug;

(4) bioactive agent which promotes healing of a tissue;

(5) anti-neoplastic drug, selected from alkylating agent (preferably cisplatin or melphalan), antimetabolite (preferably methotrexate or 5-fluorouracil), mitotic inhibitor (preferably vincristine, vinblastine, **paclitaxel** or colchicine) or hormone (preferably prednisone or tamoxifen);

(6) anti-coagulant, preferably heparin or coumarin;

(7) fibrinolytic agent, preferably streptokinase or urokinase;

(8) non-steroidal anti-inflammatory drug (NSAID), preferably ibuprofen or naproxen;

(9) steroidal anti-inflammatory drug, preferably prednisone;

(10) sodium channel blocker (preferably lidocaine or procainamide) and calcium channel blocker (preferably nifedipine or verapamil);

(11) nitric oxide donor, preferably nitroglycerin;

(12) alpha-adrenoceptor blocker, preferably phentolamine or prazosin;

(13) genetic material containing DNA and RNA;

(14) antibody;

(15) prostaglandin;

(16) leukotriene;

(17) elastin;

(18) collagen;

(19) integrin;

(20) antibiotic, preferably actinomycin D, bleomycin or rapamycin;

(21) growth factor; or

(22) radioactive molecule.

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred device: The endovascular device is selected from a **stent** (preferably balloon-expandable **stent** or self-expandable **stent**), graft and coil.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Components: (ii) is selected from 4-decyloxyphenyl diazonium chloride zinc chloride, 3-ethoxycarbonyl naphthalene diazonium tetrafluoroborate, 3,5-dichlorophenyl diazonium tetrafluoroborate, 2-chloro-4-benzamido-5-

methylbenzene diazonium chloride hemizinc chloride or 4-bromobenzene diazonium tetrafluoroborate.
Preferred Method: The step of passively depositing (iii) is carried out in an organic solvent (preferably ethanol or acetonitrile).

L122 ANSWER 6 OF 16 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-657450 [70] WPIX
CR 2003-239385 [23]; 2003-239386 [23]; 2003-289786 [28]; 2003-482075 [45]; 2003-710145 [67]; 2003-801092 [75]; 2003-829271 [77]
DNN N2002-519821 DNC C2002-184440
TI Luminal **prosthesis** useful for reducing or inhibiting **restenosis** includes a scaffold, and a device on the scaffold for releasing a substance.
DC A96 B05 B07 D22 P32
IN SIRHAN, M; YAN, J
PA (SIRH-I) SIRHAN M; (YANJ-I) YAN J; (AVAN-N) AVANTEC VASCULAR CORP
CYC 101
PI WO 2002056790 A2 20020725 (200270)* EN 97p A61F000-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
US 2002082677 A1 20020627 (200270) A61F002-06
US 2002082679 A1 20020627 (200270) A61F002-06
US 2002082685 A1 20020627 (200270) A61F002-06
US 2002114823 A1 20020822 (200270) A61F002-00
US 2002082678 A1 20020627 (200272) A61F002-06
US 6471980 B2 20021029 (200274) A61F002-02
US 2003017190 A1 20030123 (200310) A61K031-573
EP 1355588 A2 20031029 (200379) EN A61F002-06
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
ADT WO 2002056790 A2 WO 2001-US49366 20011218; US 2002082677 A1 Provisional US 2000-258024P 20001222, US 2001-782804 20010213; US 2002082679 A1 Provisional US 2000-258024P 20001222, Provisional US 2001-308381P 20010726, US 2001-2595 20011101; US 2002082685 A1 Provisional US 2000-258024P 20001222, US 2001-783253 20010213; US 2002114823 A1 Provisional US 2000-258024P 20001222, US 2001-782927 20010213; US 2002082678 A1 Provisional US 2000-258024P 20001222, US 2001-783254 20010213; US 6471980 B2 Provisional US 2000-258024P 20001222, US 2001-782927 20010213; US 2003017190 A1 Provisional US 2000-258024P 20001222, Div ex US 2001-782927 20010213, US 2002-242334 20020911; EP 1355588 A2 EP 2001-998066 20011218, WO 2001-US49366 20011218
FDT US 2003017190 A1 Div ex US 6471980; EP 1355588 A2 Based on WO 2002056790
PRAI US 2001-2595 20011101; US 2000-258024P 20001222; US 2001-782804 20010213; US 2001-782927 20010213; US 2001-783253 20010213; US 2001-783254 20010213; US 2001-308381P 20010726; US 2002-242334 20020911
IC ICM A61F000-00; A61F002-00; A61F002-02; A61F002-06; A61K031-573
ICS A61K031-365; A61K031-4745; A61K031-525
AB WO 200256790 A UPAB: 20031208
NOVELTY - A luminal **prosthesis** (13) includes a scaffold which is **implantable** within a body lumen (19), and a device (D1) on the scaffold for releasing a substance. The substance is released over a predetermined time pattern comprising an initial phase in which a substance delivery rate is below a threshold level and a subsequent phase in which the substance delivery rate is above a threshold level.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:
(1) Method for delivering a pharmacological agent to a artery

involving **implanting** a (13) that is programmed to begin substantial release of the pharmacological agent beginning after growth of at least one layer of cells over a part of the (13);

(2) A method (M1) for luminal substance delivery comprising:

(1) providing a luminal (13), which contains a matrix which undergoes degradation in a vascular environment, incorporating or coupled to the substance; and

(2) **implanting** the (13) in a (19) so that at least a portion of the matrix degrades over a time period and substantial release of substance begins after the matrix begins to degrade;

(3) A method (M2) for treatment of a patient comprising:

(1) providing a vascular (13) comprising a structure and at least one source of at least one therapeutic capable agent associated with the structure;

(2) **implanting** the vascular (13) within the patient's vasculature including a susceptible tissue site (22); and

(3) releasing the agent (A1);

(4) A method (M3) for delivering a therapeutic capable agent (A4) to a (22) within a corporeal body, comprising:

(1) positioning a source of (A4) within a vascular lumen; and

(2) releasing (A4) to the (22);

(5) A device (D2) for intracorporeal use including a structure, and at lease one source (S1) of at least one therapeutic capable agent (A5) associated with the structure; and

(6) A kit for providing a therapeutic capable agent to a (22) including: (D2) and a second compound.

ACTIVITY - Vasotropic.

MECHANISM OF ACTION - None given.

USE - For delivering a therapeutic capable agent to a (22) (claimed); and for reducing, inhibiting or treating **restenosis** and hyperplasia which may allow **angioplasty** and other interventional treatments.

ADVANTAGE - (A1) is released within a time period of 1 - 200 (preferably 1 - 45, especially 7 - 21) days from the **implanting** of the (13). The method reduces the smooth muscle cell proliferation. The device is configured to release the therapeutic capable at release rate (preferably the rate is substantially constant, decreasing, increasing or substantially non-releasing). The device delays the release of the therapeutic capable sufficiently long to allow the formation of sufficient amount of cellularization, endothelization and fibrin deposition at (22) and on the device. The luminal **prostheses** allows for programmed and controlled substance delivery with increased efficacy and/or efficacy to selected locations within a patient's vasculature to inhibit **restenosis**, minimizes drug washout and provides minimal to no hindrance to endothelization of the vessel wall. The device improves the efficiency of drug delivery by releasing a lower or minimal amount of the substance until a subsequent phase is reached, at which point the release of the substance may be substantially higher. The predetermined pattern may reduce substance loading and/or substance concentration.

DESCRIPTION OF DRAWING(S) - The figure shows a cross-sectional view of the device.

prostheses 13

expandable structure 16

body lumen 19

susceptible tissue site 22

tissue facing structure) 31

luminal facing surface. 34

Dwg.1A/11

FS CPI GMPI

FA AB; GI; DCN

MC CPI: **A12-V02**; B03-C; B04-B03A; B04-C01; B04-C02; B04-C03B; B04-C03C; B04-C03D; B04-G01; B05-A03A; B05-A03B; B05-B01J; B06-A01; B06-A03; B06-D02; B06-D03; B06-D09; B06-D13; B06-E05; B06-F03;

B07-A02A; B07-F01; B10-A13B; B10-C04B; B11-C04A; **B12-M10A**; **D09-C01**; D09-C01C

TECH UPTX: 20021031

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Device: The scaffold is a **stent** or graft. The scaffold is **implantable** in a blood vessel. (D1) includes a matrix formed over at least a portion of the scaffold. The matrix is composed of a material, which undergoes degradation in a **vascular** environment. The matrix degrades surface or bulk degradation. (S1) is configured to provide (A5) to a targeted intracorporeal site (preferably lumen or body organ) within an intracorporeal body. (D2) is configured for **implanting** at the targeted intracorporeal site supplying blood to a (22). The targeted intracorporeal site includes a (22). (D2) comprises a **vascular** (13). The **vascular** (13) comprises an expandable structure (16), graft, **stent** and a scaffold formed at least in part from an open lattice. The (16) has a luminal, a tissue facing structure (31) and an interior. (S1) is (A5). (A5) is associated with the (16) on at least one of the (16) luminal or (31), or (A5) is associated with the interior of the (16). The (16) is formed from an at least partially degradable material, which is at least partially biodegradable comprising a metal or alloy (preferably stainless steel) degradable in the corporeal body. (A5) is made available to the (22) as the stainless steel degrades within the corporal body over time. (A5) units are disassociated over time in the corporeal body, or **vascular** environment. (S1) is disposed adjacent at least one of the luminal or (31)s of the (16). (S1) comprises a rate-controlling element (C1) disposed adjacent at least a portion of the (S1) or (16). At least a portion of (C1) forms a matrix with (A5). (C1) forms the outer most layer of (D2). (D2) further includes a second rate-controlling element (C2) disposed adjacent at least a portion of (C1). (A5) is released by diffusion through (C1). (C1) includes several layers, of which at least one layer includes (A5). (S1) is a reservoir disposed adjacent to the (16). The reservoir is at least partially on an exterior, or in the interior of the (16). The reservoir is at least partially on or both the luminal and the (31)s of the (16). The reservoir is at least partially in (16). (C1) is at least partially adjacent or over the reservoir. (C1) has thickness of 10 nm - 100 microm (preferably 100 nm - 50 microm, especially 100 nm - 10 microm). (D2) further comprises a biocompatible outer layer. (D2) is configured to release (A5) in an intracorporeal body at a rate of 0.001 - 200 (preferably 1 - 100, especially 10 - 60) microg/day, at different phases (preferably at an initial phase having a lower or higher rate of release than a subsequent phase, especially either at an initial phase having an initial rate of release of 0 - 99 (preferably 0 - 75, especially 0 - 50%) of a subsequent rate of release of a subsequent phase; or at an initial phase having an initial rate of release of 0 - 50 (preferably 0.1 - 30, especially 1 - 20) microg/day, and a subsequent phase having a subsequent rate of release of 0.01 - 200 (preferably 1 - 100) microg/day or at an initial phase having an initial rate of release of 10 - 300 (preferably 40 - 300, especially 40 - 200) microg/day, and a subsequent phase having a subsequent rate of release of 0.1 - 100 (preferably 0.5 - 40, especially 0.5 - 40) microg/day). (D2) is configured to release (A5) at a substantially constant rate of 0.01 - 200 mug/day or at a total amount of 0.1 microg - 10 g (preferably 0.1 microg - 10 mg, especially 50 microg - 1 mg). (D2) is configured to deliver (A5) at a phase to a (22) of a mammalian intracorporeal body to effectuate a mammalian tissue concentration of 0.001 mug - 100 microg (preferably 1 microg - 100 microg, especially 0 ng - 10 microg) of therapeutic capable agent/mg of tissue or is configured to release (A5) at a phase to a mammalian intracorporeal body to effectuate a mammalian blood concentration of 1 ng - 50 microg (preferably 1 ng - 20 microg, especially 2 ng - 12 microg) therapeutic capable agent/ml of blood. The phase (preferably first phase) is within the first 24 hours after the **implantation** of the device in the mammalian intracorporeal body. The concentration is a peak concentration.

(D2) is configured to deliver (A5) at a second phase to the (22) of the mammalian intracorporeal body to effectuate a mammalian tissue concentration of 0.001 ng - 100 microg (preferably 1 ng - 10 microg) of therapeutic capable agent/mg of tissue. At the initial phase the release of the (A5) is delayed. The duration of the initial phase is configured to last less than 24 weeks (preferably less than 12 weeks or 1 hour - 24 weeks, especially 1 hour - 8 weeks, particularly 1 day - 1 week) or subsequent phase is configured to 1 hours - 12 weeks (preferably 4 hour - 8 week, especially 1 hour - 1 day) or 1 day - 12 weeks (preferably 2 - 45 days, especially 3 - 30 days) or 3 days - 50 weeks. (D2) is configured to deliver (A5) at the initial phase to a (22) of a mammalian intracorporeal body to effectuate a mammalian tissue concentration of the therapeutic capable agent of 10 ng/mg - 100 microg/mg. (D2) is configured to have a termination phase delivering (A5) to a mammalian intracorporeal body at a rate less than a rate of clearance (preferably 1 - 100, especially 10 or 80 ng/mg of tissue/day) the intracorporeal body of (A5). The termination phase has a duration of 14 days. (S1) is associated with the (16) by coating, spraying, dipping, vapor deposition, plasma deposition, or painting of the source onto or in the (16). (S1) is mixed in a solvent selected from methanol, dimethylsulfoxide or CO2.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Method: The substance is coated, sprayed, dipped, deposited, or painted on the (13). (M2) further involves reducing **smooth muscle cell** proliferation at the (22), releasing at least another compound (A2) and administering a second compound (A3) to the patient independent of that provided with the device. (A2) is released prior to, concurrent, or sequentially with (A1). The device is configured to release (A1) at a total amount of 0.1 microg - 10 g (preferably 1 microg - 2 mg, especially 50 microg - 1 mg). (A4) releases at a pre-determined time period following the position of the source. Step (b2) involves delaying the release of (A4) for a sufficiently long period of time to allow sufficient generation of intimal tissue to reduce occurrence of thrombotic event. The source of (A4) comprises a rate-controlling element. (A4) releases by surface or bulk degradation, hydrolysis of the source, or by diffusion through the source. (M3) alternatively involves positioning a device comprising a structure and (A4) with the structure, at a targeted intracorporeal site within a corporeal body; releasing (A4) at the targeted intracorporeal site; and further directing energy (E1) at the device to effect release (A4) from the device. The targeted intracorporeal site includes a (22) and supplies blood to a (22). The device is positioned within the corporeal body (preferably (19) or organ) during a **vascular** intervention.

(E1) is at least one of ultrasound, magnetic resonance imaging, magnetic field, radio frequency, temperature change, electromagnetic, x-ray, heat, vibration, gamma radiation, and/or microwave. Preferred Components: (A1) is immunosuppressants, anti-inflammatories, anti-proliferatives, anti-**migratory** agents, anti-fibrotic agents, proapoptotics, calcium channel blockers, anti-neoplastics, antibodies, anti-thrombotic agents, anti-platelet agents, IIb/IIIa agents and/or antiviral agents, (preferably mycophenolic acid, mycophenolate mofetil, mizoribine, methylprednisolone, dexamethasone, Certican, rapamycin, Triptolide, Methotrexate, Benidipine, Ascomycin, Wortmannin, LY294002, Camptothecin, Topotecan, hydroxyurea, Tacrolimus (FK 506), cyclophosphamide, cyclosporine, daclizumab, azathioprine, prednisone, Gemcitabine, and/or their derivatives). (A2) is an enabling compound. (A2) is a therapeutic capable agent (preferably anti-cancer agent, chemotherapeutic agent, thrombolytic, vasodilator, antimicrobials or antibiotics antimitotics, growth factor antagonists, free radical scavenger, biologic agent, radiotherapeutic agent, radiopaque agent, radiolabelled agent, anti-coagulants (including heparin or its derivative), anti-angiogenesis drug, angiogenesis drug, PDGF-B and/or EGF inhibitor, anti-inflammatory including psoriasis drugs, anti-platelet agent (preferably cyclooxygenase inhibitor such as acetylsalicylic acid, ADP inhibitor, ticlopdipine, phosphodiesterase III inhibitor, glycoprotein IIb/IIIa agents, eptifibatides, and adenosine reuptake inhibitor), healing

and/or promoting agents including anti-oxidants, nitrogen oxide donor, antiemetics, antinauseants, and/or their derivatives, especially heparin or its derivative, Thalidomide, riboflavin, tiazofurin, zafurin, acetylsalicylic acid, clopidogrel such as Plavix, ticlopdipine such as ticlid, cilostazol such as Pletal, abciximab such as Rheopro, eptifibatide such as Integrilin, dipyridmoles, non-steroid antiinflammatory drugs (NSAID), **Taxol**, Actinomycine D , and/or their derivatives). (A3) is ondansetron such as Zofran, dronabinol such as Marinol, and/or ganisetron hydrochloride such as Kytril. (A5) comprises a polymeric material formed at least in part from (A5). (A5) comprises at least one agent selected from (A1). (A5) has more than one therapeutic effect such as anti-inflammatory immunosuppressive, and anti-proliferative effect. At least one agent of (A5) includes an active compound, its pro-drug, metabolite, and/or derivative. (S1) further includes (A2) (particularly NSAID (non-steroidal antiinflammatory drug), **Taxol** or Actinomycine D, or a magnetic particle). (D2) is configured to release (A5) in response to an external source of the energy (E1) (preferably magnetic field). The second compound is (A5) and/or (A2), antiemetics, or antinauseants (preferably (A3)).

TECHNOLOGY FOCUS - POLYMERS - Preferred Components: (S1) is a polymeric material including the therapeutic capable units associated with a polymeric backbone or a metallic backbone. (C1) is formed from a material selected from polymerics, metallics, bioactive compounds, or non-bioactive compounds (preferably a polymeric material (especially poly(lactic acid), poly(glycolic acid) and copolymers, poly dioxanone, poly(ethyl glutamate), poly(hydroxy butyrate), polyhydroxyvalerate and copolymers, polycaprolactone, polyanhydride, poly(ortho esters), poly(iminocarbonates), polycyanoacrylates, polyphosphazenes, copolymers and other aliphatic polyesters, or their copolymers including copolymers of poly-L-lactic acid and poly-e-caprolactone, their mixtures and/or copolymers, polyurethane, polyethylenes imine, cellulose acetate butyrate, ethylene vinyl alcohol copolymer, silicone, polytetrafluoroethylene (PTFE), parylene, parylast, poly(methyl methacrylate butyrate), poly-N-butyl methacrylate, poly(methyl methacrylate), poly 2-hydroxy ethyl methacrylate, poly ethylene glycol methacrylate, poly vinyl chloride, poly(dimethyl siloxane), poly(tetrafluoroethylene), poly (ethylene oxide), poly ethylene vinyl acetate, poly carbonate, poly acrylamide gel, N-vinyl-2-pyrrolidone, maleic anhydride, Nylon, cellulose acetate butyrate (CAB), other synthetic or natural polymeric substances, mixtures and their copolymers, particularly silicone, PTFE, parylast, polyurethane, parylene, cellulose acetate butyrate, and/or their copolymers), a biodegradable material, a non-biodegradable, slow degrading material, a natural material (especially fibrin, albumin, collagen, gelatin, glycosoaminoglycan, chondroitin, oligosaccharide and polysaccharide, phosholipid, phosphorylcholine, glycolipid, protein, amino acid, cellulose, and/or copolymers), or a metallic material (especially material selected from at least two titanium, chromium, Nitinol, stainless steel, and/or alloys and having different galvanic potential). The bio-compatible layer is formed from a material containing polyethylene glycol, polyethylene oxide, hydrogels, silicone, polyurethanes, and/or heparin.

TECHNOLOGY FOCUS - BIOLOGY - Preferred Method: The **cells** are inflammatory **smooth muscle** or endothelial **cells**.

ABEX UPTX: 20021031

ADMINISTRATION - (A3) is administered orally, pulmonarily, systemically, transdermally, and/or through any bodily orifice. (A3) is administered in a dosage of 0.5 - 5 g (preferably 2 - 3 g, especially 1 - 3 mg or 2 - 6 mg) per day. (A3) is administered prior to, concurrent with, or subsequent to, the interventional procedure (preferably either 200 days prior to - 200 days after, especially 30 days prior to - 30 days after, particularly 1 day prior to - 30 days after; or 200 days prior to about up to the interventional procedure, especially 3 months prior to about up to the

interventional procedure, particularly 7 days - 24 hours prior to the interventional procedure) (claimed).

EXAMPLE - DuraflexTM (a stainless steel **stent**) having a dimension of 3x14 mm was sprayed with a solution of therapeutic capable agent (25 mg/ml) in 100% ethanol or methanol solvent. The **stent** was dried and the ethanol was evaporated leaving the agent on the **stent** surface. A poly-l-lactic acid/poly-e-caprolactone copolymer (75:25) was prepared in 1,4-dioxane. The agent coated **stent** was loaded on a mandrel rotating at 200 rpm and a spray gun used to dispense the copolymer solution in a fine spray onto the coated **stent**, as the **stent** rotated for 10 - 30 second time period. The **stent** was then placed in an oven at 25 - 35 degrees C for up to 24 hours to complete the evaporation of the solvent.

L122 ANSWER 7 OF 16 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-589126 [63] WPIX
CR 1998-086713 [08]; 2002-361049 [39]; 2003-558843 [52]
DNN N2002-467412 DNC C2002-166678
TI **Stented** graft for delivering medicinal agents, comprises **stent** and flexible, porous, biocompatible tubular elastomeric covering and is coated with polymer and therapeutic substance.
DC A96 B07 D22 P32
IN SHANNON, D T
PA (SHAN-I) SHANNON D T
CYC 1
PI US 2002042645 A1 20020411 (200263)* 27p A61F002-06
ADT US 2002042645 A1 Div ex US 1996-675644 19960703, CIP of US 1999-358350 19990721, US 2001-997829 20011129
PRAI US 2001-997829 20011129; US 1996-675644 19960703; US 1999-358350 19990721
IC ICM A61F002-06
AB US2002042645 A UPAB: 20030813
NOVELTY - A drug eluting **stented** graft comprises:

(a) a **stent** (S) (14), which is in compact configuration with a first diameter, expanded configuration with greater diameter and lateral openings (19); and

(b) a flexible, porous, biocompatible tubular elastomeric covering (EC) (16) coated with composite coat of polymer (P) and therapeutic substance (TS).

DETAILED DESCRIPTION - A drug eluting **stented** graft comprises:

(a) a **stent** (S) (14), which is cylindrical with an outer surface and hollow bore extending longitudinally and exists in compact configuration with a first diameter, expanded configuration with greater diameter and lateral openings (19); and

(b) a flexible, porous, biocompatible tubular elastomeric covering (EC) (16) having a first and second end, outer surface and hollow bore that also extends longitudinally to form inner surface.

S is deployed coaxially within hollow bore, so that the inner surface of the covering is in contact with outer surface of S and it is coated with a composite coat of polymer (P) and therapeutic substance (TS).

INDEPENDENT CLAIMS are also included for the following:

(1) a method for treating cardiovascular (CVS) diseases, which involves **implanting** graft to patient to ameliorate symptom(s) of CVS disease; and

(2) an article comprising the graft within a packaging material with a label which indicates the device is ready for **implantation**.

USE - For **implanting** in cavities or passage-ways (ducts or blood vessels) of body for releasing agents, such as antiplatelet agent, anticoagulant agent, antimetabolic agent, vaso-active agent, nitric oxide releasing agent, antiinflammatory agent, antiproliferative agent, antisense agent, proendothelial agent, antimigratory agent, antimicrobial

agent, selective gene delivery vectors (such as Semliki forest virus (SMV) adapted to deliver **restenosis** preventing genes), sirolimus, actinomycin-D and/or **paclitaxel**.

ADVANTAGE - The graft is highly flexible, has high hoop strength in expanded form, minimal foreshortening of strength, minimal dog-born effect, minimal puckering, wrinkling or invagination of elastomer graft material during transition from compressed to expanded state. The graft is smoothly inserted in convolutions and EC is firmly laminated or fused to permanent relative of move individual members of S without tearing or rapturing of tubular graft. The polymer has controlled degree of hydrophobicity in environment of use and erodes into innocuous products at continuous rate without exhibiting deleterious effects on environment or animal body, is safe and easily releases agents.

DESCRIPTION OF DRAWING(S) - The figure shows enlarged, cut-elevational view of drug eluting **stented** graft.

Stent 14
Elastomeric covering 16
Lateral openings 19

Dwg.2/9

FS CPI GMPI

FA AB; GI; DCN

MC CPI: A12-V01; **A12-V02**; A12-V03B; B02-A; B04-C03; B04-E06; B05-A01B; B05-A03A; B05-A03B; B05-C07; B06-A03; B06-E05; B07-H; B09-H; B10-A03; B11-C04A; B11-C06; **B12-M10**; B12-M11E; B14-C03; B14-F01; B14-F02; B14-F06; B14-H01B; B14-L06; D09-C

TECH UPTX: 20021001

TECHNOLOGY FOCUS - POLYMERS - Preferred Polymer: P is bioerodible polymer, polyester or hydrophobic copolymer comprising mers (I), (II), (III) or (IV).

R1 = di-, tri- or tetravalent radicals having 1-10C alkylene, 2-10C alkenylene, 2-6C alkyleneoxy, or 3-7C cycloalkylene, arylene or 4-7C cycloalkenylene optionally substituted with T or 1-10C alkylene;
T = 1-7C alkyl, 1-7C alkoxy or 2-7C alkenyl;
a = 0 or 1;
b = 2 - 6;
m, n, p = greater than 10; and
R2, R3 = T, alkoxy, OR1O, 2-7C alkenyloxy, 2-6C alkylene(oxy), 3-6C alkenylene(oxy), aryloxy, 8-12C aralk(en)yleneoxy, oxa, OR1O, 5-8C heterocyclic or 8-12C fused polycyclic ring with O atom (optionally substituted with T) when R2 and R3 are taken together.

Preferred Properties: TS bioerodes and releases the therapeutic at a zero order rate, continuous rate, or variable rate. The rate is produced is by preselecting P, TS and EC to give desired results. Several microcapsules containing therapeutic agents are dispersed within (IV) and they have walls made of drug release rate controlling material. The polymer is a biocompatible nonbioerodible polymer that sequesters an agent for branchytherapy, such as palladium-103 (103Pd), 192Ir, 32P, 188Re or Sr/Y90 source trains.

Preferred Elastomers: EC is polytetrafluoroethylene, fluorinated ethylene propylene, polytetrafluoroethylene-perfluoroalkyl vinyl ether copolymer, polyvinyl chloride, polypropylene, polyethylene terephthalate, broad fluoride or other biocompatible plastics. E is formed of expanded, sintered polytetrafluoroethylene (PTFE) tape having fibrils of length 300, preferably 5 microns. The width of the tape is less than 1, preferably 0.015 inch.

TECHNOLOGY FOCUS - MECHANICAL ENGINEERING - Preferred Arrangements: S has elements (E) with undulating linear cylinder with cylinder axis aligned on axis of the bore. Each E is spiral and connected to adjacent neighbor E. The linear shape is a zig-zag shape with tips which lies in plane with tip of adjacent neighbor E or is sinusoidal shape with peaks and valleys whose adjacent neighbor lie in common plane. The length dimension is 3 - 10 times greater than width and depth dimension. S and EC are anchored to

each other by a unit with protrusions of covering that protrude into lateral openings of S. The tape is wound around S in overlapping fashion, so that EC comprises 1 - 10 layers of tape (with width of 0.5 inches (1.27 cm)), or is helically wrapped on S, so that 6 - 8 revolutions of tape are applied per longitudinal inch (2.54 cm) of graft. S comprises a shape memory alloy that alternately exists in a first and a second crystalline state. S assumes a radially expanded configuration and radially compact configuration when the shape memory alloy is in the first and the second crystalline state, respectively. S is formed of a metal alloy comprising at least two E, such as iron, cobalt, chromium, nickel, titanium, niobium or molybdenum. The alloy comprises (wt.%) nickel (at least 51 - 59%), chromium (0.25%) and titanium.

EC has a thickness of less than 0.1 inch and the PTFE tape has density of less than 1.6 g/cc. S is radially collapsible to a diameter which is equal to first diameter and radially expandable to a diameter which is equal to second diameter of graft. The lateral openings exists in S when S is at its radially expanded second diameter, continuous, tubular PRFE covering formed on S.

Preferred Method: S is immersed in a liquid composite dispersion, removed and remaining dried. The coating is formed by electron beam deposition and a tubular covering is then adherent to the coat.

L122 ANSWER 8 OF 16 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2002-566630 [60] WPIX
DNN N2002-448571 DNC C2002-160598
TI Polymer-based drug delivery composition for delivery of therapeutic agents, comprises biocompatible block copolymer comprising elastomeric block(s) and thermoplastic block(s), loaded with therapeutic agent.
DC A96 B07 D22 P34
IN KAMATH, K; NOTT, S; PINCHUK, L; SCHWARZ, M
PA (KAMA-I) KAMATH K; (NOTT-I) NOTT S; (PINC-I) PINCHUK L; (SCHW-I) SCHWARZ M; (SCIM-N) SCIMED LIFE SYSTEMS INC
CYC 98
PI WO 2002047731 A2 20020620 (200260)* EN 47p A61L000-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
US 2002107330 A1 20020808 (200260) C08L033-02
AU 2002030851 A 20020624 (200267) A61L000-00
US 6545097 B2 20030408 (200327) C08L023-00
EP 1341565 A2 20030910 (200367) EN A61L027-34
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
US 2003171496 A1 20030911 (200367) C08F002-00
ADT WO 2002047731 A2 WO 2001-US48380 20011212; US 2002107330 A1 US 2000-734639 20001212; AU 2002030851 A AU 2002-30851 20011212; US 6545097 B2 US 2000-734639 20001212; EP 1341565 A2 EP 2001-991102 20011212, WO 2001-US48380 20011212; US 2003171496 A1 Cont of US 2000-734639 20001212, US 2002-319802 20021213
FDT AU 2002030851 A Based on WO 2002047731; EP 1341565 A2 Based on WO 2002047731; US 2003171496 A1 Cont of US 6545097
PRAI US 2000-734639 20001212; US 2002-319802 20021213
IC ICM A61L000-00; A61L027-34; C08F002-00; C08L023-00; C08L033-02
ICS A61K009-22; A61L031-04; A61L031-10; A61L031-16; C08L023-04
AB WO 200247731 A UPAB: 20020919
NOVELTY - Polymer-based drug delivery composition comprises biocompatible block copolymer loaded with therapeutic agent. The copolymer comprises elastomeric block(s) and thermoplastic block(s).
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) medical device, portion(s) of which is insertable or

implantable into the body of the patient and comprises the block copolymer loaded with the therapeutic agent; and

(2) a coated medical device comprising an intravascular or intervascular medical device provided with the coating composition.

USE - For delivery of therapeutic agent such as anti-thrombotic agent, anti-thrombotic agent, anti-sense DNA, anti-sense RNA (claimed).

ADVANTAGE - Polymer-based drug delivery composition has good mechanical integrity, good biocompatibility e.g. vascular compatibility, as demonstrated by the tendency to provoke minimal adverse tissue reactions as demonstrated by reduced polymorphonuclear leukocyte and reduced macrophage activity. The polymers are homocompatible and have ability to minimize thrombotic occlusion of small vessel as demonstrated by coating such polymers on coronary **stents**. The copolymer has high tensile strength, resistance to cracking and other forms of degradation under in-vivo conditions.

DESCRIPTION OF DRAWING(S) - The figure shows the release rate as a function of time for **stents** coated with polystyrene-polyisobutylene-polystyrene copolymer and **paclitaxel** in varying ratios.

Dwg.1/2

FS CPI GMPI

FA AB; GI; DCN

MC CPI: A12-V01; **A12-V02**; B04-C01; B04-C02; B04-C03; B04-E01; B11-C04A; **B12-M10A**; B14-C03; B14-C07; B14-F02; B14-F02D; B14-F04; B14-F06; B14-H01; **D09-C01**

TECH UPTX: 20020919

TECHNOLOGY FOCUS - POLYMERS - Preferred Composition: The block copolymer is of formula, X-(AB)n.

A = elastomeric block, preferably polyolefin block of formula (-CRR'-CH2)n;

R, R' = aliphatic or cyclic aliphatic groups;

B = thermoplastic block, preferably vinyl aromatic block or a methacrylate polymer block;

n = positive integer; and

X = seed molecule.

The polyolefin block comprises an isobutylene monomer and vinyl aromatic polymer block comprising monomer(s) such as styrene or alpha-methylstyrene. B comprises monomer(s) selected from methylmethacrylate, ethylmethacrylate and hydroxyethyl methacrylate. The block copolymer contains 95-45 mol% of polyolefin blocks. The loaded block copolymer comprises 0.1-70 weight% of therapeutic agent and 0.1-75 weight.% of **paclitaxel**. The block copolymer is provided as a coating 0.1-15 micron, preferably 0.1-40 microns thickness over portion(s) of a medical device. The medical device further comprises (co)polymer of polycarboxylic acid, cellulose acetate polymer, cellulose nitrate polymer, gelatin, polyvinylpyrrolidone, cross-linked polyvinylpyrrolidone, polyanhydride, polyamide, polyvinyl alcohol, polyvinyl ether, polyvinyl aromatic, polyethylene oxide, glycosaminoglycan, polysaccharide, polyester, polyacrylamide, polyether, polyether sulfone, polycarbonate, polyalkylene, halogenated polyalkylene, polyurethane, polyorthoester, polypeptide, silicon, siloxane polymer, polylactic acid, polyglycolic acid, polycaprolactone, polyhydroxybutyrate valerate, fibrin, collagen, collagen derivative or a hyaluronic acid, preferably polyacrylic acid, ethylene-vinyl acetate copolymer and copolymer of polylactic acid and polycaprolactone. The copolymer is blended with or provided in a layer of biocompatible block copolymer.

Preferred Properties: The block copolymer has molecular weight of 80000-300000 Daltons. The polyolefin block has molecular weight of 60000-200000. The vinyl aromatic polymer block has molecular weight of 20000-100000. The therapeutic agent is released over an extended period after **implantation** in a patient. The medical device is adapted such that at least a portion of the block copolymer is exposed to bodily fluid or tissues upon insertion or **implantation** in the body.

Preferred Medical Device: The medical device is a **catheter**, guide wire, balloon, filter, **stent**, **stent** graft, vascular graft, vascular patch, shunt or intraluminal paving system. The device is preferably a **stent** or **catheter** further comprising a sheath for covering the block copolymer during inserting into the body to prevent premature therapeutic agent release. The device is adapted for **implantation** or insertion into coronary vasculature, peripheral vascular system, esophagus, trachea, colon, biliary tract, urinary tract, prostate or brain.
Preferred Therapeutic Agent: The therapeutic agent is selected from anti-thrombotic agent, anti-thrombotic agent, anti-proliferative agent, anti-inflammatory agent, anti-migratory agent, agent affecting extracellular matrix production and organization, anti-neoplastic agent, anti-mitotic agent, anesthetic agent, anti-coagulant, vascular cell growth promoter, vascular cell growth inhibitor, cholesterol-lowering agent, vasodilating agent, agent that interferes with endogenous vasoactive mechanisms, anti-sense DNA, anti-sense RNA, DNA coding for anti-sense RNA, DNA coding for tRNA or rRNA, DNA coding for angiogenic factors, DNA coding for cell cycle inhibitors DNA coding for cell proliferation inhibition agents, and DNA coding for bone morphogenic proteins, analogous cells, allogeneic cells and xenogeneic cells.

ABEX UPTX: 20020919

EXAMPLE - A **stent** was coated with solution containing 94 % toluene, 5 % tetrahydrofuran (THF), and 1 % polystyrene-polyisobutylene-polystyrene copolymer (PPPC)-**paclitaxel** combination. The solution was formed by mixing **paclitaxel** and THF, into which the copolymer, toluene were added, mixed thoroughly and filtered. Biocompatibility was studied by **implanting** in a porcine coronary artery, bare stainless steel NIR **stent**, NIR **stent** coated with traditional biostable polycarbonate urethane polymer, NIR **stent** having coating of traditional copolymer of polylactic acid and polyglycolic acid and NIR **stent** coated with the PPPC. After 28 days, the **stent** was harvested from the animal and examined for **stenosis** and inflammation. **Stenosis** (in %), in bare **stent**, polycarbonate urethane and PPPC was respectively 43, 75 and 47 and the inflammation was respectively 2.6, 3.9 and 1.5 respectively. **Stenosis** and inflammation were significantly higher with **stents** coated with traditional polycarbonate urethane polymer than with the bare **stents** or **stents** coated with PPPC.

L122 ANSWER 9 OF 16 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2001-541065 [60] WPIX
CR 2001-513821 [56]; 2001-565070 [63]; 2003-491673 [46]
DNN N2001-402145 DNC C2001-161435
TI Coating composition for **implantable** device or **prosthesis**, e.g. **stent**, contains ethylene vinyl alcohol copolymer and isopropyl alcohol/water solvent.
DC A17 A96 B07 D22 G02 P34 P42
IN BHAT, V D; CHEN, Y; GURUWAIYA, J A; HOSSAINY, S F A; MANDRUSOV, E; MIRZAEE, D; SANDERS-MILLARE, D; SHAH, A
PA (ADCA-N) ADVANCED CARDIOVASCULAR SYSTEM; (BHAT-I) BHAT V D; (CHEN-I) CHEN Y; (GURU-I) GURUWAIYA J A; (HOSS-I) HOSSAINY S F A; (MAND-I) MANDRUSOV E; (MIRZ-I) MIRZAEE D; (SAND-I) SANDERS-MILLARE D; (SHAH-I) SHAH A
CYC 94
PI US 2001018469 A1 20010830 (200160)* 19p C08K003-00
WO 2001074414 A1 20011011 (200161) EN A61L027-54
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

AU 2001053831 A 20011015 (200209) A61L027-54
ADT US 2001018469 A1 CIP of US 1999-470559 19991223, CIP of US 2000-540242 20000331, CIP of US 2000-621123 20000721, US 2000-750655 20001228; WO 2001074414 A1 WO 2001-US40223 20010302; AU 2001053831 A AU 2001-53831 20010302
FDT AU 2001053831 A Based on WO 2001074414
PRAI US 2000-750655 20001228; US 1999-470559 19991223; US 2000-540242 20000331; US 2000-621123 20000721
IC ICM A61L027-54; C08K003-00
ICS A61L027-34; A61L029-08; A61L029-16; A61L031-10; A61L031-16; B05D003-00
AB US2001018469 A UPAB: 20030719
NOVELTY - A coating composition consists of an ethylene vinyl alcohol copolymer which is dissolved in an isopropyl alcohol/water solvent.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a method of forming a coating for a **prosthesis** by utilizing the specified composition.
USE - For **implantable** medical device or **prosthesis**, e.g. balloon-expandable **stent**, self-expandable **stent**, and grafts (claimed).
ADVANTAGE - The coating composition strongly adheres to the surface of the **prosthesis**, preventing significant loss of polymeric coating during **prosthesis** delivery. It allows for a significant control of the release rate of an active agent.
Dwg.0/6
FS CPI GMPI
FA AB; DCN
MC CPI: A08-S02; A10-E09B2; **A12-V02**; B02-D; B04-C03B; B06-A03; B11-C04; **B12-M10**; B14-F02; D09-C; G02-A05
TECH UPTX: 20011018
TECHNOLOGY FOCUS - POLYMERS - Preferred Composition: The composition also includes an active agent carried by the copolymer to inhibit abnormal or inappropriate migration or proliferation of smooth muscle cells and to inhibit **restenosis** of a blood vessel.
Preferred Components: The copolymer is Soarnol (RTM) and comprises 27-29 mole % ethylene. It acts as an intermediate tie layer between a metallic surface of the **prosthesis** and a coating layer carrying the active agent, and/or as a diffusion barrier disposed over the coating layer to control the release rate of active agent. The active agent is actinomycin D, **paclitaxel**, docetaxel, its analogs, or its derivatives.
ABEX UPTX: 20011018
EXAMPLE - An ethylene vinyl alcohol solution was made by dissolving Soarnol D-2908 (RTM) (0.2 g) in isopropyl alcohol/water solvent (9.73 g). Actinomycin-D was added to the solution, and the solution was vortexed and placed in a vial. A **stent** was cleaned in an ultrasonic bath of isopropyl alcohol solution for 10 minutes, dried, and plasma cleaned in a plasma chamber. The **stent** was coated with the solution by passing the **stent** under spray head for 3-10 seconds, interpass dried using warm air at 45 degrees C, and final dried in an oven at 50 degrees C. The average dried coating on the **stent** was 200-600 mug with an estimated actinomycin D concentration of 50-140 mug/ **stent**.

L122 ANSWER 10 OF 16 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2001-475649 [51] WPIX
CR 2000-587124 [55]; 2001-091750 [10]; 2002-556413 [59]; 2003-615989 [58]
DNC C2001-142565
TI Solid composition for delivery of active agents e.g. glyburide comprises carrier optionally containing a substrate having an encapsulation coat containing hydrophilic surfactants e.g. polyoxyethylene alkylethers.
DC A96 B05 B07
IN CHEN, F; PATEL, M V

PA (LIPO-N) LIPOCINE INC; (CHEN-I) CHEN F; (PATE-I) PATEL M V
CYC 95
PI WO 2001037808 A1 20010531 (200151)* EN 106p A61K009-14
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
US 6248363 B1 20010619 (200151) A61K009-16
AU 2001017981 A 20010604 (200153) A61K009-14
EP 1233756 A1 20020828 (200264) EN A61K009-14
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
US 2003064097 A1 20030403 (200325) A61K009-20
US 6569463 B2 20030527 (200337) A61K009-16
JP 2003517470 W 20030527 (200344) 118p A61K009-48
US 2003215496 A1 20031120 (200377) A61K009-48
ADT WO 2001037808 A1 WO 2000-US32255 20001122; US 6248363 B1 US 1999-447690 19991123; AU 2001017981 A AU 2001-17981 20001122; EP 1233756 A1 EP 2000-980761 20001122, WO 2000-US32255 20001122; US 2003064097 A1 Div ex US 1999-447690 19991123, US 2001-800593 20010306; US 6569463 B2 Div ex US 1999-447690 19991123, US 2001-800593 20010306; JP 2003517470 W WO 2000-US32255 20001122, JP 2001-539423 20001122; US 2003215496 A1 Div ex US 1999-447690 19991123, Cont of US 2001-800593 20010306, US 2003-428341 20030501
FDT AU 2001017981 A Based on WO 2001037808; EP 1233756 A1 Based on WO 2001037808; US 2003064097 A1 Div ex US 6248363; US 6569463 B2 Div ex US 6248363; JP 2003517470 W Based on WO 2001037808; US 2003215496 A1 Div ex US 6248363, Cont of US 6569463
PRAI US 1999-447690 19991123; US 2001-800593 20010306; US 2003-428341 20030501
IC ICM A61K009-14; A61K009-16; A61K009-20; A61K009-48
ICS A61K009-02; A61K009-22; A61K009-28; A61K009-32; A61K009-46; A61K009-50; A61K009-51; **A61K009-52**; **A61K009-54**; **A61K009-56**; A61K009-58; A61K031-216; A61K031-232; A61K031-351; A61K031-366; A61K031-40; A61K031-404; A61K031-415; A61K031-4196; A61K031-421; A61K031-436; A61K031-4409; A61K031-4439; A61K031-4725; A61K031-522; A61K031-57; A61K031-64; A61K031-663; A61K038-23; A61K047-02; **A61K047-10**; A61K047-14; A61K047-22; A61K047-26; A61K047-28; A61K047-32; A61K047-36; A61K047-38; A61K047-44; A61P001-04; A61P003-04; A61P003-06; A61P003-10; A61P005-16; A61P005-24; A61P005-40; A61P007-02; A61P007-10; A61P009-04; A61P009-06; A61P009-10; A61P009-12; A61P013-08; A61P015-10; A61P017-12; A61P019-06; A61P019-10; A61P021-02; A61P025-04; A61P025-06; A61P025-08; A61P025-16; A61P025-20; A61P025-22; A61P025-26; A61P025-28; A61P029-00; A61P031-04; A61P031-10; A61P031-12; A61P033-06; A61P033-10; A61P035-00; A61P037-06; A61P043-00
AB WO 200137808 A UPAB: 20031128
NOVELTY - Composition for improved delivery of active agent comprising a solid carrier optionally containing a substrate having an encapsulation coat, where the solid carrier or encapsulation coat contains at least one active agent (I) and one hydrophilic surfactant (II), is new.
ADVANTAGE - The composition is used to deliver a wide variety of active agents having improved absorption and/or biovailability. It provides coated substrate materials without the need for binders. Prior art solid carriers are limited to a few specific drugs due to difficulties in formulating appropriate drug/exicipient compositions to effectively coat the active agent onto a carrier particle. Most of prior art solid dosage forms of hydrophilic active agents exhibit poor or no absorption of the active agent. Non-solid formulations of the same are chemically instable, leak and have capsule shell incompatibility. Conventional solid

dosage forms of hydrophobic active agents often exhibit slow and incomplete dissolution and subsequent absorption. They often show a high propensity for biovariability and food interactions of the active agent, resulting in restrictive compliance/labeling requirements. A comparative dissolution study was performed on 3 forms of glyburide (Ia) namely coated beads of (Ia), commercially available (Ia) and pure (Ia) bulk. 5 mg Of each form was usd for triplication dissolution runs in 500 ml of isotonic pH 7.4 phosphate buffer.The dissolutiom medium was sampled at 15, 30, 45, 60, 120 and 180 minutes. The samples were filtered and the filtrates diluted for (Ia)-specific HPLC assay. The (Ia)-coated beads showed a superior dissolution profile in the rate, extent and variability of (Ia) dissolved/released into the medium.

Dwg.0/3

FS CPI

FA AB; DCN

MC CPI: A10-E08; A12-V01; A12-W12C; B01-C04; B01-D01; B01-D02; B03-H; B04-B01C1; B04-C02D; B04-C02X; B04-C03C; B04-D01; B04-N04; B05-B01P; B06-D05; B07-H; B10-A08; B10-A09A; B10-A09B; B10-A22; B10-C04D; B10-C04E; B12-M07; B12-M08; B12-M09; **B12-M10**; B12-M11

TECH UPTX: 20010910

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Composition: (I) is a drug, a nutrient, a cosmeceutical and/or a diagnostic agent. The substrate may be an additive and/or an active agent. (I) may be hydrophobic having an intrinsic aqueous solubility of less than 1 mg/ml. (I) may be hydrophilic with an apparent water solubility of at least 1 mg/ml. Hydrophilic (I) is selected from a drug, cytokine, peptidomimetic, peptide, protein, toxoid, serum, antibody, vaccine, nucleoside, nucleotide, genetic material and/or nucleic acid. The encapsulation coat further comprises at least one lipophilic additive selected from lipophilic surfactants and/or triglycerides. The composition is encapsulated, extruded, compressed, pelletized, coated, mixed, granulated, crystallized, Iyophilized or molded. It may be formulated as a capsule, a tablet, an ovule, a suppository, a wafer, a chewable tablet, a buccal tablet, a sub-lingual tablet, a quick-dissolve tablet, an effervescent tablet, a granule, a pellet, a bead, a pill, a sachet, a sprinkle, a film, a dry syrup, a reconstitutable solid, a suspension, a lozenge, a troche, an **implant**, a powder, a triturate, a platelet, or a strip. It may be formulated for immediate release, pulsatile release, controlled release, extended release, delayed release, targeted release, or targeted delayed release.

Preferred Substrate: The substrate is a powder or a multiparticulate. It may be an additive comprising a solubilizer, an enzyme inhibitor, an anti-adherent, an anticoagulant, an antifoaming agent, an antioxidant, a binder, a bufferant, a chelating agent, a coagulant, a colorants or opaquants, a coolant, a cryoprotectant, a diluent or filler, a disintegrant or super disintegrant, a hydrogen bonding agent, a flavorant or desensitizer, an ion-exchange resin, a plasticizer, a preservative, a solvent, a sweetener and/or a thickener. the substrate is a multiparticulate comprised of a granule, a pellet, a bead, a spherule, a beadlet, a microcapsule, a millisphere, a nanocapsule, a nanosphere, a microsphere, a platelet, a tablet or a capsule.

Preferred Carrier: The carrier is a bead, a beadlet, a granule, a spherule, a pellet, a microcapsule, a microsphere, a nanosphere, a film, a wafer, a sprinkle, an **implant**, a troche, a lozenge, a platelet, a nanocapsule or a strip. It is enteric coated, coated for fast disintegration, seal coated, film coated, barrier coated, compress coated, or coated with an enzyme-degradable coating.

Preferred Lipophilic Additive: The lipophilic additive is selected from alcohols, polyoxyethylene alkylethers, fatty acids, bile acids, glycerol fatty acid esters, acetylated glycerol fatty acid esters, lower alcohol fatty acids esters, polyethylene glycol fatty acids esters, polyethylene glycol glycerol fatty acid esters, polypropylene glycol fatty acid esters, polyoxyethylene glycerides, lactic acid derivatives of mono/diglycerides,

propylene glycol diglycerides, sorbitan fatty acid esters, polyoxyethylene sorbitan fatty acid esters, polyoxyethylenepolyoxypropylene block copolymers, transesterified vegetable oils, sterols, sterol derivatives, sugar esters, sugar ethers, sucroglycerides, polyoxyethylene vegetable oils, polyoxyethylene hydrogenated vegetable oils, reaction mixtures of polyols and at least one fatty acid, glyceride, optionally hydrogenated vegetable oils, and/or sterols. The triglyceride is selected vegetable oils, fish oils, animal fats, hydrogenated vegetable oils, partially hydrogenated vegetable oils, synthetic triglycerides, modified triglycerides, and/or fractionated triglycerides.

Preferred Surfactant: (II) is a non-ionic surfactant (IIa) having an hydrophilic-lipophilic balance (HLB) value of at least 10 or an ionic surfactant (IIb). (IIa) is selected from alkylglucosides, alkylmaltosides, alkylthioglucosides, lauryl macrogolglycerides, polyoxyethylene alkyl ethers, alkylphenols, or sorbitan fatty acid esters, polyethylene glycol glycerol fatty acid esters, polyoxyethylene- polyoxypropylene block copolymers, polyglycerol fatty acid esters, polyoxyethylene glycerides, polyoxyethylene sterols, polyoxyethylene vegetable oils, polyoxyethylene hydrogenated vegetable oils and/or reaction mixtures of polyols and at least one fatty acid, glyceride, vegetable oil, hydrogenated vegetable oil, and sterol, tocopherol polyethylene glycol succinate, sugar ester, sugar ether and/or sucroglycerides. (IIb) is selected from alkyl ammonium salts, bile acids and their salts, or derivatives, fatty acid derivatives of amino acids, carnitines, oligopeptides, and polypeptides, glyceride derivatives of amino acids, oligopeptides, and polypeptides, acyl lactylates, mono-or diacetylated tartaric acid esters of mono- or diglycerides, succinylated monoglycerides, citric acid esters of mono- or diglycerides, alginate salts, propylene glycol alginate, optionally hydrogenated lecithins, optionally hydrogenated lysolecithins, lysophospholipids, phospholipids, alkylsulfate salts, fatty acid salts and/or sodium docusate.

TECHNOLOGY FOCUS - POLYMERS - Preferred Surfactant: (II) is a non-ionic surfactant (IIa) having an hydrophilic-lipophilic balance (HLB) value of at least 10 or an ionic surfactant (IIb). (IIa) is selected from alkylglucosides, alkylmaltosides, alkylthioglucosides, lauryl macrogolglycerides, polyoxyethylene alkyl ethers, alkylphenols, or sorbitan fatty acid esters, polyethylene glycol glycerol fatty acid esters, polyoxyethylene- polyoxypropylene block copolymers, polyglycerol fatty acid esters, polyoxyethylene glycerides, polyoxyethylene sterols, polyoxyethylene vegetable oils, polyoxyethylene hydrogenated vegetable oils and/or reaction mixtures of polyols and at least one fatty acid, glyceride, vegetable oil, hydrogenated vegetable oil, and sterol, tocopherol polyethylene glycol succinate, sugar ester, sugar ether and/or sucroglycerides. (IIb) is selected from alkyl ammonium salts, bile acids and their salts, or derivatives, fatty acid derivatives of amino acids, carnitines, oligopeptides, and polypeptides, glyceride derivatives of amino acids, oligopeptides, and polypeptides, acyl lactylates, mono-or diacetylated tartaric acid esters of mono- or diglycerides, succinylated monoglycerides, citric acid esters of mono- or diglycerides, alginate salts, propylene glycol alginate, optionally hydrogenated lecithins, optionally hydrogenated lysolecithins, lysophospholipids, phospholipids, alkylsulfate salts, fatty acid salts and/or sodium docusate.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Active Agent: (I) is selected from hydrophobic agents that are analgesics, anti-inflammatory agents, anthelmintics, anti-arrhythmic agents, anti-bacterial agents, anti-viral agents, anti-coagulants, anti-depressants, anti-diabetics, anti-epileptics, anti-fungal agents, anti-gout agents, anti-hypertensive agents, anti-malarials, anti-migraine agents, anti-muscarinic agents, anti-neoplastic agents, erectile dysfunction improvement agents, immunosuppressants, anti-protozoal agents, anti-thyroid agents, anxiolytic agents, sedatives, hypnotics, neuroleptics, D-Blockers, cardiac inotropic agents, corticosteroids, diuretics, anti-parkinsonian agents, gastro-intestinal agents, histamine receptor antagonists, keratolytics,

lipidregulating agents, anti-anginal agents, COX-2 inhibitors,leucotriene inhibitors, macrolides, muscle relaxants, nutritional agents, opioid analgesics, protease inhibitors, sex hormones, stimulants, muscle relaxants, anti-osteoporosis agents,anti-obesity agents, cognition enhancers, anti-urinary incontinence agents, nutritional oils, anti-benign prostate hypertrophy agents, essential fatty acids and/or non-essential fatty acids. (I) is selected from acutretin, albendazole, albuterol, aminogluthemide, amiodarone, arniodipine, amphetamine, amphotericin B, atorvastatin, atovaquone, azithromycin, bactofen, beclomethsone, benezepril, benzonatate, betamethasone, bicalutanide, budesonide, bupropion, busulphan, butenafine, calcifediol, calciprotiene, calcitriol, camptothecan, candesartan, capsaicin, carbamezepine, carotenes, celecoxib, cerivistatin, cetrizine, chlorpheniramine, cholecalciferol, cilostazol, cimetidine, cinnarizine, ciprofloxacin, cisapride, clarithromycin, clemastine, clormphene, clornipramine, clopidrogel, codeine, coenzyme Q10, cyclobenzaprine, cyclosporine, danazol, dantrolene, dexchlopheniramine, diclofenac, dicournarol, digoxin, dihydroepiandrosterone, dihydroergotamine, dihydrotachysterol, dirithromycin, donepezil, efavirenz, eposartan, ergocalciferol, ergotarnine, essential fatty acid sources, etodolac, etoposide, famotidine, fenofibrate, fentanyl, fexofenadine, finasteride, flucanazole, flurbiprofen, fluvastatin, fosphenytion, frovatriptan, furazolidone, gabapentin, gemfibrozil, glibenclamide, glipizide, glyburide, glymepride, griseofulvin, halofantrine,lbuprofen, irbesartan, irinotecan, isosorbide dinitrate, isotreinoin, itraconazole, ivermectin, ketoconazoie, ketorolac, lamotrigine, lanosprazole, leflunomide, lisinopril,loperamide, loratadine, lovastatin, L-thryroxine, lutein, lycopene, medroxyprogesterone,mefepristo ne, mefloquine, megesterol acetate, methadone, methoxsalen, metronidazole, metronidazole, miconazole, midazolam, miglitol, minoxidil, mitoxantrone, montelukast, nabumetone, nalbuphine, naratiptan, nelfinavir, nifedipine, nilsolidipine, nilutanide, nitrofurantoin, nizatidine, orneprazole, oprevelkin, osteradiol, oxaprozin, **paclitaxel**, paricalcitol, paroxetine, pentazocine, pioglitazone, pizofetin, pravastatin, prednisolone, probucol, progesterone, pseudo-ephedrine, pyridostigmine, rabeprazole, raloxifene, refocoxib, repaglinide, rifabutine, rifapentine, rimexolone, ritanovir, rizatriptan, rosigiltazone, saquinavir, sertraline, sibutramine, sildenafil citrate, simvastatin, sirolimus, spironolactone, sumatriptan, tacrine, tacrolimus, tamoxifen, tamsulosin, targretin,tazarotene, telmisartan, teniposide, terbinafine, terzosin, tetrahydrocannabinol, tiagabine,ticlidopine, tirofibran, tizanidine, topiramate, topotecan, toremifene, trarnadol, tretinoin, troglitazone, trovafloxacin, ubidecarenone, valsartan, venlafaxine, vertoporfin, vigabatrin, vitamin A, vitamin D, vitamin E, vitamin K, zafirlukast, zileuton, zolmitriphan, zolpidem and/or zopiclone. (I) may also be selected from acarbose, acylovir, acetylcysteine, acetylcholine chloride, alatrofloxacin, alendronate, alglucerase, amantadine hydrochloride, ambenomium, amifostine, amiloride hydrochloride, aminocaproic acid, amphotericin B, antihemophilic factor (human), antihemophilic factor (porcine), antihemophilic factor (recombinant), aprotinin, asparaginase, atenolol, atracurium besylate, atropine, azithromycin, aztreonam, BCG vaccine, bacitracin, becalermin, belladona, bepridil hydrochloride, bleomycin sulfate, calcitonin human, calcitonin salmon, carboplatin, capecitabine, capreomycin sulfate, cefamandole nafate, cefazolin sodium, cefepime hydrochloride, cefixime, cefonicid sodium, cefoperazone, cefotetan disodium, cefotoxime, cefoxitin sodium, ceftizoxime, ceftriaxone, cefuroxime axetil, cephalexin, cephapirin sodium, cholera vaccine, chrionic gonadotropin, cidofovir, cisplatin, cladribine, clidinium bromide, clindamycin and clindamycin derivatives, ciprofloxacin, clondronate, colistimethate sodium, colistin sulfate, cortocotropin, cosyntropin, cromalyn sodium, cytarabine, daltaperin sodium, danaproid, deforoxamine, denileukin diftitox, desmopressin, diatrizoate megluamine and diatrizoate sodium, dicyclomine, didanosine, dirithromycin, dopamine hydrochloride, domase alpha, doxacurium chloride, doxorubicin, editronate

disodium, elanaprilat, enkephalin, enoxacin, enoxaprin sodium, ephedrine, epinephrine, epoetin alpha, erythromycin, esmol hydrochloride, factor IX, famiciclovir, fludarabine, fluoxetine, foscarnet sodium, ganciclovir, granulocyte colony stimulating factor, granulocyte-macrophage stimulating factor, growth hornone-recombinant human, growth hormone-bovine, gentamycin, glucagon, glycopyrolate, gonadotropin releasing hormone and synthetic analogs, GnRH, gonadorelin, grepafloxacin, hemophilus B conjugate vaccine, Hepatitis A virus vaccine inactivated, Hepatitis B virus vaccine inactivated, heparin sodium, indinavir sulfate-, influenza virus vaccine, interleukin-2, interleukin-3, insulin-human, insulin lispro, insulin procine, insulin NPH, insulin aspart, insulin glargine, insulin detemir, interferon alpha, interferon beta, ipratropium bromide, isofosfamide, japanese encephalitis virus vaccine, lamivudine, leucovorin calcium, leuprolide acetate, levofloxacin, lincomycin and lincomycin derivatives, lobucavir, lomefloxacin, loracarbef, mannitol, measles virus vaccine, meningococcal vaccine, menotropins,mephenzolate bromide, mesalmine, methanamine, methotrexate, methscopolamine, metformin hydrochloride, metroprolol, mezocillin sodium, rnivacurium chloride, mumps, viral vaccine, nedocromil sodium, neostigmine bromide, neostigmine methyl sulfate, neutontin, norfloxacin, octreotide acetate, ofloxacin, olpadronate, oxytocin, pamidronate disodium, pancuronium bromide, paroxetine, pefloxacin, pentarnindine isethionate, pentostatin, pentoxifylllne, periciclovir, pentagastrin, phentolarnine mesylate, phenylalanine, physostigmine salicylate, plague vaccine, piperacillin sodium, platelet derived growth factor-human, pneumococcal vaccine polyvalent, poliovirus vaccine inactivated, pollovirus vaccine live (OPV), polymixin B sulfate, pralidoxine chloride, pramlintide, pregabalin, propofenone, propenthaline bromide, pyridostigmine bromide, rabies vaccine, residronate, ribavarin, rimantadine hydrochloride, rotavirus vaccine, salmetrol xinafoate, sincalide, small pox vaccine, solatol, somatostatin, sparfloxacin, spectinomycin, stavudine, streptokinase, streptozocin, suxamethoniurn chloride, tacrine hydrochloride, terbutaline sulfate, thiopeta, ticarcillin, tiludronate, timolol, tissue type plasminogen activator, TNFR:Fc, TNK-tPA, trandolapril, trimetrexate gluconate, trospectinomycin, trovafloxacin, tubocurarine chloride, tumor necrosis factor, typhoid vaccine live, urea, urokinase, vancomycin, valaciclovir, valsartan, varicella virus vaccine live, vasopressin and vasopressin derivatives, vecoronium bromide, vinblastin, vincristine, vinorelbine, vitamin B12 , warfarin sodium, yellow fever vaccine, zalcitabine, zanamavir, zolandronate, and/or zidovudine.

ABEX UPTX: 20010910

ADMINISTRATION - The composition is formulated for oral, nasal, ocular, urethral, buccal, transmucosal, vaginal, topical or rectal delivery (claimed). Dosage not given.

EXAMPLE - A composition was prepared containing (g): glyburide (1); PEG-4 stearate (33), glycerol monolaurate (17) and non-pareil seed (30/35 mesh) (80). The composition was formulated as coated beads.

L122 ANSWER 11 OF 16 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2001-355746 [37] WPIX
DNC C2001-110358
TI Composition for sustained percutaneous delivery of active agent, comprises active agent in charged polymer matrix forming in vivo, particularly alginate.
DC B04 B07
IN JOHNSON, M S; MCLENNAN, G
PA (ADRE-N) ADVANCED RES & TECHNOLOGY INST; (JOHN-I) JOHNSON M S; (MCLE-I) MCLENNAN G
CYC 23
PI WO 2001037802 A1 20010531 (200137)* EN 33p A61K009-00
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
W: AU CA US

AU 2001019318 A 20010604 (200153) A61K009-00
EP 1233751 A1 20020828 (200264) EN A61K009-00
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE TR
US 2003021848 A1 20030130 (200311) A61K009-14
ADT WO 2001037802 A1 WO 2000-US32467 20001129; AU 2001019318 A AU 2001-19318 20001129; EP 1233751 A1 EP 2000-982263 20001129, WO 2000-US32467 20001129; US 2003021848 A1 WO 2000-US32467 20001129, US 2002-148047 20020524
FDT AU 2001019318 A Based on WO 2001037802; EP 1233751 A1 Based on WO 2001037802
PRAI US 1999-167834P 19991129; US 2002-148047 20020524
IC ICM A61K009-00; A61K009-14
ICS A61K038-00; A61K047-36
AB WO 200137802 A UPAB: 20021031
NOVELTY - Composition comprises an active agent contained within a matrix capable of forming in-vivo, comprising a biological compatible polymer having at least 2 charged parts of the same charge. The polymer is crosslinked with at least 1 biologically compatible multivalent counter-ion.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for the preparation of the composition.

USE - Used for sustained delivery of active agents e.g. for preventing or treating **restenosis**.

Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B04-C03; **B12-M10A**; B14-F02D
TECH UPTX: 20010704
TECHNOLOGY FOCUS - POLYMERS - Preferred compounds: The charged parts of the same charge of the polymer are negatively charged, and the polymer is preferably an alginate, especially sodium alginate.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred compounds: The active compound is a drug, preferably an anticancer agent comprising **paclitaxel**, cisplatin and/or adriamycin, gene, antibody, preferably an antivascular endothelial growth factor, fatty acid, preferably triglyceride or lipoprotein comprising HDL, heparin, or a protein, preferably a monocyte chemotactic protein, or an angiogenic protein comprising vascular endothelial growth factor, carbohydrate preferably polysaccharide comprising glycosaminoglycan, a starch, sucrose, glucose, lactose, maltose, fructose and/or cellobiose, a vector preferably adenovirus, plasmid and/or retrovirus, cell preferably a natural killer cell, T cell, B cell, red blood cell, white blood cell and/or macrophage, and/or nucleic acid. Preferred composition: The multivalent counter ions are provided by the active agent, preferably proteins provide the counter ions to crosslink the polymer having negative charges or they may be provided by an independent source preferably calcium, magnesium and/or manganese salts, particularly calcium gluconate.
The composition comprises heparin and an alginate.
The multivalent counter-ion to polymer IE ratio is 0.2-2 (preferably 0.58).

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: Preparation of the composition comprises combining the biologically active compound and polymer, preferably in liquid form, with polymer dissolved in water. The polymer and multi-valent counter-ions are combined in-vivo, or are combined immediately before percutaneous delivery.
ABEX UPTX: 20010704
ADMINISTRATION - Administration is percutaneous, e.g. via a hypodermic needle to a desired internal locus.
EXAMPLE - One femoral and both carotid arteries of 11 swine were **angioplastied** to 20% over dilation. 0.2 ml Heparin suspended in 1.6 ml 1% sodium alginate solution, was injected into the periadventitial space at the site of **angioplasty**. Calcium gluconate (0.2 ml) was

then injected to crosslink the alginate. In each animal, 1 injection was of titrated heparin (2micro-Ci/4000U), 1 injection was of unlabelled heparin (4000U), and 1 injection was of fluoroisothiocyanate-labelled heparin (2000U). Two animals were sacrificed initially, 1 on day 1, and 2 animals on each of days 3, 7, 14 and 21.
The average amount of heparin recovered at all time points was 12 times that of the recovery from control vessels. At 21 days, 0.5 and 0.1 units of heparin were present within the artery at the **angioplasty** site.

L122 ANSWER 12 OF 16 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2001-191488 [19] WPIX
DNC C2001-057377
TI **Implantable** active agent depot, useful e.g. in local tumor treatment or gene therapy, comprising drug-containing, cubic phase forming lipid matrix containing modifier molecule to control release kinetics.
DC A96 B07
IN RESZKA, R; SCHLUETER, R
PA (DELB-N) DELBRUCK CENT MOLEKULARE MEDIZIN MAX; (DELB-N) DELBRUECK CENT MOLEKULARE MEDIZIN MAX
CYC 95
PI WO 2001010411 A2 20010215 (200119)* DE 13p A61K009-127
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
DE 10038203 A1 20010503 (200126) A61K031-282
AU 2000075044 A 20010305 (200130) A61K009-127
EP 1204407 A2 20020515 (200239) DE A61K009-127
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
CN 1368874 A 20020911 (200282) A61K009-127
HU 2002002299 A2 20021228 (200308) A61K009-127
JP 2003506397 W 20030218 (200315) 25p A61K009-127
ADT WO 2001010411 A2 WO 2000-DE2615 20000804; DE 10038203 A1 DE 2000-10038203 20000804; AU 2000075044 A AU 2000-75044 20000804; EP 1204407 A2 EP 2000-963870 20000804, WO 2000-DE2615 20000804; CN 1368874 A CN 2000-811369 20000804; HU 2002002299 A2 WO 2000-DE2615 20000804, HU 2002-2299 20000804; JP 2003506397 W WO 2000-DE2615 20000804, JP 2001-514931 20000804
FDT AU 2000075044 A Based on WO 2001010411; EP 1204407 A2 Based on WO 2001010411; HU 2002002299 A2 Based on WO 2001010411; JP 2003506397 W Based on WO 2001010411
PRAI DE 1999-19938331 19990806
IC ICM A61K009-127; A61K031-282
ICS A61K009-22; A61K031-132; A61K031-337; A61K031-437; A61K031-485; A61K031-704; A61K031-7072; A61K031-7105; A61K031-711; A61K033-24; A61K038-00; A61K045-00; A61K047-24; A61K047-34; A61K048-00; **A61P009-10**; A61P025-04; A61P025-16; A61P025-28; A61P029-00; A61P035-00
AB WO 200110411 A UPAB: 20010405
NOVELTY - An **implantable** active agent depot comprises a lipid matrix which can form cubic phases, incorporating modifier molecules (I) and containing pharmaceutically active agents (A).
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:
(1) methods for production of the depot, involving (i) combining the lipid matrix, (I) and (A) or (ii) adding (I) and optionally lipid-soluble (A) to the lipid matrix then mixing with an aqueous phase containing water-soluble (A); and
(2) methods for using the depot, in which (i) the depot is applied to biodegradable netting, (ii) the depot releases antiangiogenetic agents and genetic materials influencing these systems or (ii) the depot releases

angiogenetic agents and materials influencing these systems.

USE - The use of the depot is claimed for: (a) local chemotherapy or gene therapy of tumor diseases (e.g. glioblastoma, brain metastases, peritonal carcinosis, bladder carcinoma or breast cancer recurrence); (b) for treating arteriosclerotic vascular walls (e.g. **restenosis**); (c) for treating Parkinson's disease, Alzheimer's disease or multiple sclerosis; (d) as a slow release system for analgesics (e.g. morphine); (e) for treating rheumatic disease (e.g. rheumatoid arthritis); and (f) for releasing antiinflammatory agents. Typically a depot containing at least one chemotherapeutic agent can be applied locally as a gel after surgical removal of the main mass of a tumor, to improve the prospects of prolongation of life and the quality of life.

ADVANTAGE - A rational membrane design is provided, which allows fine control of the release of (A) over time and the amount of (A) released. Typically (A) can be released over 4 days or 7 days using (I) based on PEG-500 or PEG-2000 respectively; geometric factors (e.g. the surface and volume of the sample) can also be used to control release. The depot systems are completely biodegradable, can be applied to open tissue (e.g. after operations) and adhere well to mucosa, e.g. to provide effective local treatment of tumors or prevention of **restenosis**. The cubic phase lipid system is relatively stable towards contact with body fluids; is easily handled (due to the high viscosity); adheres well to biological tissue; and contains 3-dimensional internal water channels, which can incorporate water-soluble (A) (e.g. carboplatin) in a form which is protected from direct contact with body fluids (to prevent degradation by macrophages and enzymes) but can be released slowly by diffusion.

Dwg.0/4

FS CPI

FA AB; DCN

MC CPI: A12-V01; B02-T; B04-A07A; B04-B03C; B04-C01; B04-C03; B04-E01; B05-A03B; B05-B01P; B06-E05; B07-A02A; B07-D12; B08-D02; **B12-M10**; B14-C01; B14-C03; B14-C09B; B14-F07; B14-H01B; B14-J01A3; B14-J01A4; B14-S01; B14-S03

TECH UPTX: 20010405

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: The lipid matrix is of monoolein. (I) are lipid molecules having a charged or sterically bulky negatively head group. (I) is especially the negatively charged head group 1,2-dimyristoyl-glycerophosphatidic acid (DMPA, sodium salt); or an amphiphilic molecule with a polyethylene glycol (PEG) head group of a specific length (preferably 500-2000 units), particularly 1,2-distearoyl-glycerophosphatidyl-ethanolamine-methyl polyethylene glycol (MPEG-DSPE). (A) is carboplatin, oxaliplatin, **taxol**, daunorubicin, mitoxantrone, gemcitabine, topotecan, camptothecin, a peptide or a gene-therapeutic agent (e.g. DNA, RNA, oligonucleotides or ribozymes). Combinations of (A), e.g. carboplatin and **taxol**, can also be used.

TECHNOLOGY FOCUS - POLYMERS - Preferred Materials: (I) include amphiphilic molecules with polyethylene glycol (PEG) head groups of a specific length (preferably 500-2000 units), particularly 1,2-distearoyl-glycerophosphatidyl-ethanolamine-methyl polyethylene glycol (MPEG-DSPE).

ABEX UPTX: 20010405

EXAMPLE - 27 mM of carboplatin, in the form of a 10 mg/ml solution in bidistilled water. 40 weight % of the solution was added to 5 g of molten monoolein at 45degreesC under stirring. This procedure was repeated 3 times to give a homogeneous cubic phase, followed by tempering in a closed container for 24 hours at 40degreesC to reach equilibrium. System containing 5 mol. % 1,2-dimyristoyl-glycerophosphatidic acid (DMPA, sodium salt) or 1,2-distearoyl-glycerophosphatidyl-ethanolamine-methyl polyethylene glycol (MPEG-DSPE) were prepared analogously, the additional lipid being added to the molten monoolein in powder form and dissolved by shaking before addition of the carboplatin solution. Release tests were carried out by contacting the products with distilled water at 25degreesC

and monitoring the amount of carboplatin in the supernatant by HPLC. Results showed that after 48 hours the amount released, compared with that in the absence of additional lipid, was ca. 15% higher in presence of DMPA and ca. 15% lower in presence of MPEG-DSPE.

L122 ANSWER 13 OF 16 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2001-091743 [10] WPIX
DNN N2001-069487 DNC C2001-027118
TI **Stent** having a polymeric coating for controllably releasing active agent, e.g. for inhibiting **restenosis**.
DC A23 A96 B02 B07 D22 P32
IN SMITH, S R; STANSLASKI, J L; WANG, L; YANG, D
PA (BOST-N) BOSTON SCI LTD; (SCIM-N) SCIMED LIFE SCI INC; (SCIM-N) SCIMED LIFE SYSTEMS INC
CYC 92
PI WO 2001001890 A1 20010111 (200110)* EN 19p A61F002-06
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2000057905 A 20010122 (200125) A61F002-06
EP 1107707 A1 20010620 (200135) EN A61F002-06
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
US 6258121 B1 20010710 (200141) A61F002-06
US 2001032014 A1 20011018 (200166) A61F002-06
JP 2003503153 W 20030128 (200309) 18p A61L031-00
US 6569195 B2 20030527 (200337) A61F002-06
ADT WO 2001001890 A1 WO 2000-US40105 20000606; AU 2000057905 A AU 2000-57905 20000606; EP 1107707 A1 EP 2000-943431 20000606, WO 2000-US40105 20000606; US 6258121 B1 US 1999-346975 19990702; US 2001032014 A1 Cont of US 1999-346975 19990702, US 2001-883870 20010618; JP 2003503153 W WO 2000-US40105 20000606, JP 2001-507394 20000606; US 6569195 B2 Cont of US 1999-346975 19990702, US 2001-883870 20010618
FDT AU 2000057905 A Based on WO 2001001890; EP 1107707 A1 Based on WO 2001001890; US 2001032014 A1 Cont of US 6258121; JP 2003503153 W Based on WO 2001001890; US 6569195 B2 Cont of US 6258121
PRAI US 1999-346975 19990702; US 2001-883870 20010618
IC ICM A61F002-06; A61L031-00
ICS A61K009-00; **A61M029-02**; A61P035-00
AB WO 200101890 A UPAB: 20010220
NOVELTY - A **stent** has a polymeric coating comprising a mixture of two co-polymers, for controllably releasing active agent from the coating, particularly to inhibit **restenosis**.

DETAILED DESCRIPTION - A **stent** comprises a **stent** body having a coating in which a biologically active ingredient is dispersed, where the coating comprises a mixture of a first co polymer (CP1) and a second co-polymer (CP2), where CP1 and CP2 would release the agent at different rates, and their mixture releases active ingredient at a rate between the two.

INDEPENDENT CLAIMS are included for the use of a **stent** described above, where the co-polymers are polylactic acid/polyethylene oxide (PLA-PEO) and polylactic acid/polycaprolactone (PLA/PCL), and the active agent is **paclitaxel** or an analog or derivative, for inhibiting **restenosis**.

ACTIVITY - Vasotropic.

MECHANISM OF ACTION - None given.

USE - The **stent** is used, e.g. in a coronary vessel following **angioplasty** to inhibit **restenosis**.

Dwg.0/3
FS CPI GMPI

FA AB; DCN
MC CPI: A05-E09; A05-H02; A07-A03A; A12-V03; B04-C03; B06-A03; B11-C04A; B14-F01E; **D09-C01B**
TECH UPTX: 20010220
TECHNOLOGY FOCUS - POLYMERS - Preferred Compounds: Preferably 1 co-polymer is hydrophobic and the other hydrophilic, e.g. PLA-PEO co-polymer and PLA/PCL co-polymer.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Active Agent: The active agent is preferably **paclitaxel** or an analog or derivative.

L122 ANSWER 14 OF 16 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2000-422877 [36] WPIX
DNN N2000-315584 DNC C2000-127899
TI **Implantable** medical devices with controlled release delivery of bioactive agents comprising a base material, a composite layer of a bioactive agent and a polymer, and a barrier layer..
DC A96 B07 D22 P34
IN BARRY, J J; KAMATH, K R; NOTT, S H
PA (SCIM-N) SCIMED LIFE SYSTEMS INC; (BOST-N) BOSTON SCI LTD; (BARR-I) BARRY J J; (KAMA-I) KAMATH K R; (NOTT-I) NOTT S H
CYC 91
PI WO 2000032255 A1 20000608 (200036)* EN 39p A61L029-08
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2000030999 A 20000619 (200044)
EP 1135178 A1 20010926 (200157) EN A61L029-08
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
US 6335029 B1 20020101 (200207) A61K009-00
US 2002054900 A1 20020509 (200235) A61M031-00 <--
JP 2002531183 W 20020924 (200278) 28p A61L029-00
AU 758175 B 20030320 (200329) A61L029-08
US 6589546 B2 20030708 (200353) A61F002-00
ADT WO 2000032255 A1 WO 1999-US26887 19991112; AU 2000030999 A AU 2000-30999 19991112; EP 1135178 A1 EP 1999-964984 19991112, WO 1999-US26887 19991112; US 6335029 B1 CIP of US 1998-143521 19980828, US 1998-204259 19981203; US 2002054900 A1 CIP of US 1998-143521 19980828, Cont of US 1998-204259 19981203, US 2001-6889 20011210; JP 2002531183 W WO 1999-US26887 19991112, JP 2000-584944 19991112; AU 758175 B AU 2000-30999 19991112; US 6589546 B2 CIP of US 1998-143521 19980828, Cont of US 1998-204259 19981203, US 2001-6889 20011210
FDT AU 2000030999 A Based on WO 2000032255; EP 1135178 A1 Based on WO 2000032255; JP 2002531183 W Based on WO 2000032255; AU 758175 B Previous Publ. AU 2000030999, Based on WO 2000032255; US 6589546 B2 Cont of US 6335029
PRAI US 1998-204259 19981203; US 1998-143521 19980828; US 2001-6889 20011210
IC ICM A61F002-00; A61K009-00; A61L029-00; A61L029-08; **A61M031-00**
ICS A61B017-00; A61F013-00; A61K009-14; A61K031-337; A61K047-30; A61K047-32; A61K047-34; A61K047-36; A61L029-16; A61L031-10; A61L031-16; **A61M025-00**; A61P035-00
AB WO 200032255 A UPAB: 20000801
NOVELTY - **Implantable** medical devices with controlled release delivery of bioactive agents comprising a base material, a composite layer of a bioactive agent and a polymer, and a barrier layer.
DETAILED DESCRIPTION - An **implantable** medical device comprises:
(a) a structure consisting of a base material adapted for

introduction into a patient;

(b) at least one composite layer comprising at least one bioactive agent and a polymer material applied to at least a portion of the outer surface of the base material; and

(c) at least one barrier layer positioned over the composite layer wherein the thickness of the barrier layer is adequate to provide controlled release of the bioactive agent(s) and wherein the barrier layer is formed in situ by a low energy plasma polymerization process of a monomer gas.

An INDEPENDENT CLAIM is also included for a method for the localized delivery of a drug agent to a target location within a body.

USE - The medical devices provide controlled, localized delivery of bioactive agents within the body to treat or prevent certain conditions or diseases e.g. to prevent abrupt closure and/or **restenosis** of a body portion such as a passage, lumen or blood vessel.

Dwg.0/4

FS CPI GMPI

FA AB; DCN

MC CPI: A12-V01; **A12-V02**; A12-V03D; B04-C01; B04-C02; B04-C03; B04-N04; B05-B01B; B06-A03; B11-C04; **B11-C04B**; **D09-C01**

TECH UPTX: 20000801

TECHNOLOGY FOCUS - POLYMERS - Preferred Polymer: The polymer material is preferably selected from polyurethane, polycarboxylic acids, polyorthoesters, polyvinylpyrrolidone, maleic anhydride polymers, polyamides, polyvinyl alcohols, polyethylene oxides, glycosaminoglycans, proteins, polypeptides, silicones, polysaccharides, polyesters, polyacrylamides, polyethers, copolymers of vinyl monomers and mixtures and copolymers thereof.

Preferred Base material: The base material is a metal or polymer.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Device: The device is selected from a **catheter**, guide wire, cannula, **stent** graft, covered **stent**, vascular or other graft, cardiac pacemaker lead or lead tip, an **angioplasty** device or portion thereof etc.

The composite layer is formed by dissolution, dispersion, absorption or adsorption of at least one bioactive agent and polymer material, and it form a matrix depot of the bioactive agent. The thickness of the barrier layer is at less than 5000, preferably about 50-2000 angstroms. The device may comprise a further drug layer over the barrier layer wherein the drug layer may comprise heparin or additional bioactive material which may be introduced into the barrier layer by a dipping process.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Monomer Gas: The monomer gas is selected from cyclic or acyclic siloxane silicon-based monomers, silane silicon-based monomers, silylimidazoles silicon-based monomers, hydrofluorocarbon-based monomers, aliphatic or aromatic hydrocarbon-base monomers, acrylic monomers and combinations thereof.

Preferred Bioactive Agent: At least 1 bioactive agent is **paclitaxel**.

ABEX UPTX: 20000801

EXAMPLE - None given.

L122 ANSWER 15 OF 16 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN

AN 2000-224531 [19] WPIX

DNC C2000-068615

TI Method of inhibiting injury to vascular tissue comprising local administration of antiangiogenic agent.

DC B05 D16

IN BROWN, C L; GORLIN, S

PA (GLOB-N) GLOBAL VASCULAR CONCEPTS INC

CYC 87

PI WO 2000010552 A2 20000302 (200019)* EN 29p A61K031-00

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES
FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS
LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ
TM TR TT UA UG UZ VN YU ZA ZW

AU 9956871 A 20000314 (200031) A61K031-00

ADT WO 2000010552 A2 WO 1999-US19218 19990824; AU 9956871 A AU 1999-56871 19990824

FDT AU 9956871 A Based on WO 2000010552

PRAI US 1998-97579P 19980824

IC ICM A61K031-00

AB WO 200010552 A UPAB: 20000419

NOVELTY - A new method of inhibiting injury to vascular tissue comprises local administration of an anti-angiogenic agent.

ACTIVITY - Antiarteriosclerosis; cardiant; vasotropic; antianginal, cerebroprotective; cytostatic.

MECHANISM OF ACTION - None given.

USE - The vascular injury is due to atherosclerosis, cardiac transplant vasculopathy, coronary **restenosis** following coronary intervention, balloon **angioplasty**, **stent** placement, rotablator, carotid endarterectomy, dialysis graft **stenosis**, graft anastomosis neointima, unstable angina, acute myocardial infarction, stroke, benign hypertrophy or benign prostatic hypertrophy, particularly atherosclerosis or **restenosis**.

Dwg.0/6

FS CPI

FA AB; DCN

MC CPI: B01-A02; B01-C04; B01-D02; B02-T; B04-B04L; B04-B04M; B04-C02; B04-C03; B04-G01; B04-H01; B04-H02A; B04-H02N; B04-H05A; B04-H08; B04-J01; B04-N02; B04-N06; B05-A03B; B05-B01G; B06-A01; B06-A03; B06-D01; B06-D03; B06-D04; B06-E05; B07-A02B; B07-A03; B07-B01; B07-D03; B07-D04; B07-D10; B07-D13; B07-E01; B10-A10; B10-A13D; B10-A18; B10-B01B; B10-C02; B10-C03; B10-C04E; B10-D03; B14-E11; B14-F01B; B14-F01E; B14-F02D; B14-F04; B14-F07; B14-H01B; B14-N16; D05-H11

TECH UPTX: 20000419

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred drugs: The antiangiogenic agent is selected from AGM-1470 (TNP-470), antibody to vascular endothelial growth factor or fibroblast growth factor, batimastat (BB-94), marimastat, tyrosine kinase inhibitor, genistein, SU5416, integrin antagonist alphaVbeta3/5, retinoid, retinoic acid fenretinide, 11 alpha-epihydrocortisol, corteloxone, tetrahydrocortisone, 17 alpha-hydroxyprogesterone, protein kinase inhibitor, staurosporine, MDL 27032, 22-oxa-1-alpha, 25-dihydroxyvitamin D3, arachidonic acid inhibitor, indomethacin, sulindac, tetracycline, minocycline, thalidomide, estradiol, 2-methoxyestradiol, tumor necrosis factor-alpha, interferon-gamma-inducible protein 10, interleukin 1 and interleukin 12, interferon alpha, beta or gamma, Angiostatin protein, plasminogen fragment, Endostatin protein, collagen fragment, proliferin-related protein, group B streptococcus toxin, CM101, CM, troponin I, squalamine, nitric oxide synthase inhibitor, L-NAME, thrombospondin, wortmannin, amiloride, spironolactone, ursodeoxycholic acid, bufalin, suramin, tecogalan sodium, linoleic acid, captopril, irsogladine, FR-118487, triterpene acid, castanospermine, leukemia inhibitory factor, lavendustin A, platelet factor-4, herbimycin A, diaminoantraquinone, **taxol**, aurintricarboxylic acid, DS-4152, pentosan polysulfite, radicicol, fragments of human prolactin, erbstatin, eponemycin, shark cartilage, protamine, Louisianin A, C and D, PAF antagonist WEB 2086, auranofin, ascorbic ether, sulfated polysaccharide D4152, anti-keloid agent and TRANILAST.

ABEX UPTX: 20000419

ADMINISTRATION - The anti-angiogenic agent is administered via a

catheter, is incorporated into a locally administered polymer or is incorporated into a **stent** or **stent** coating or an endovascular graft or endovascular graft coating which is placed locally on the tissue. When administered via a **catheter** the agent is incorporated into endoluminal paving of a **catheter** which is directed locally to the tissue. The polymer permits local sustained release of the agent.

L122 ANSWER 16 OF 16 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1999-385766 [32] WPIX
DNC C1999-113577
TI Local delivery of therapeutic agents - using **implants**, **stents** and **catheters**..
DC B02 B03 B07
IN WRENN, S M
PA (SUPE-N) SUPERGEN INC
CYC 26
PI WO 9930684 A1 19990624 (199932)* EN 54p A61K009-00
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA CN HU IL JP
AU 9914031 A 19990705 (199948) A61K009-00
EP 1037605 A1 20000927 (200048) EN A61K009-00
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI NL PT SE
US 6485514 B1 20021126 (200281) A61F002-06
ADT WO 9930684 A1 WO 1998-US24151 19981112; AU 9914031 A AU 1999-14031 19981112; EP 1037605 A1 EP 1998-957882 19981112, WO 1998-US24151 19981112; US 6485514 B1 US 1997-989281 19971212
FDT AU 9914031 A Based on WO 9930684; EP 1037605 A1 Based on WO 9930684
PRAI US 1997-989281 19971212
IC ICM A61F002-06; A61K009-00
AB WO 9930684 A UPAB: 19990813
NOVELTY - A new **implant** for administering a therapeutic agent comprises an **implant** structure and a cytotoxic or cytostatic agent.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:
(1) a method of treatment comprising inserting the novel **implant** into a lumen in a body;
(2) a kit comprising an **implant** and a mechanism capable of inserting it into a lumen of a body;
(3) a **stent** comprising a cytotoxic or cytostatic agent;
(4) a method of treatment comprising administering a therapeutic agent through an intraluminal **catheter**.
ACTIVITY - Cytotoxic; cytostatic.
MECHANISM OF ACTION - None given.
USE - The **implant** is useful for the local delivery of therapeutic agents for the treatment of **restenosis**, cancers, insults to body tissue due to surgery, diseases that produce fibrosis of tissue, repetitive motion disorders, disorders of tissues that are not highly vascularised and proliferative responses associated with organ transplants.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B06-A03; B06-D18; B06-E05; B11-C04; B12-M10B; B14-F02; B14-H01B; B14-N17
TECH UPTX: 19990813
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: The **implant** is preferably a time-release **implant** composed of a gel or polymer and may be formed in situ. The theraputic agent preferably interrupts cell replication of prevents or limits chemotaxis. Preferred Drugs: The theraputic agent is preferably camptothecin, **taxol**, methotrexate, mitoxantrone, etoposide, colchicine, azathioprine, vincristine, vinblastine, fluorouracil, adriamycin or

mitomycin.

ABEX UPTX: 19990813

EXAMPLE - A **stent** was coated with a dispersion of 9-nitro-20(S)-camptothecin in 1% poly(L-lactic acid) in chloroform and delivered in an artery at or near a tumor site.

Considered 11/29/04

=> d his

(FILE 'HOME' ENTERED AT 08:32:18 ON 20 JAN 2004)
SET COST OFF

FILE 'REGISTRY' ENTERED AT 08:33:43 ON 20 JAN 2004
L1 1 S TAXOL/CN
L2 62 S 33069-62-4/CRN

FILE 'HCAPLUS' ENTERED AT 08:36:48 ON 20 JAN 2004
L3 7962 S L1 OR L2
L4 10727 S TAXOL OR PACLITAXEL OR PLAXICEL OR YEWTAXAN# OR TAXALBIN# OR
E STENT/CT
E E10+ALL
L5 1534 S E2
L6 2466 S STENT
E BLOOD VESSEL/CT
L7 9801 S E41
L8 22486 S VASCULAR(L)SMOOTH(L)MUSCLE
L9 15220 S VASCULAR(L)SMOOTH(L)MUSCLE(L)CELL
E ANGIOPLASTY/CT
E E3+ALL
L10 2708 S E2
E ANGIOPLAST
L11 4247 S E9
E RESTENOSIS/CT
E E3+ALL
L12 3406 S E2,E3
L13 5196 S RESTENOSIS
E STENOSIS/CT
L14 6 S E3
E E2+ALL
L15 1013 S E12
E MUSCLE CELL/CT
E CELL MIGRATION/CT
L16 15070 S E3
E E3+ALL
E E10+ALL
E PROSTHE/CT
L17 27060 S E36,E37
L18 1078 S E66,E67
L19 316 S E62
L20 32 S E43
L21 12082 S E57
E E37+ALL
E IMPLANT/CT
E E12+ALL
L22 1837 S E2
L23 12082 S E8
E CATHETER/CT
L24 104 S E5
E E5+ALL
L25 2425 S E2
L26 147 S L3 AND L5,L6,L17-L25
L27 143 S L3 AND L7-L15
L28 34 S L3 AND L16

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L29          165 S L4 AND L5,L6,L17-L25
L30          171 S L4 AND L7-L15
L31          522 S L7 AND L16
L32           76 S L26,L29 AND L27,L28,L30,L31
L33           72 S L3,L4 AND SUSTAIN?(L)RELEAS?
L34          282 S L3,L4 AND (SUSTAIN? OR CONTROL?)(L)(RELEAS? OR ACTION?)
L35           24 S L33,L34 AND L32
                 E SCIMED/PA,CS
L36          216 S E3-E22
                 E KUNZ L/AU
L37           72 S E3,E6,E11,E12
                 E KLEIN R/AU
L38          418 S E3,E4
L39           41 S E60,E62,E63
                 E RENO J/AU
L40           95 S E3,E5,E8,E12,E13
                 E GRAINGER D/AU
L41           82 S E3,E5,E8,E11,E12
                 E METCALFE J/AU
L42          302 S E3,E6,E14,E15
                 E WEISSBERG P/AU
L43           80 S E3-E6
                 E ANDERSON P/AU
L44          131 S E3,E14
                 E ANDERSON PETE/AU
L45           61 S E3,E4,E10
L46           18 S L36-L45 AND L3,L4
L47           14 S L46 AND L5-L35
L48            4 S L46 NOT L47
L49            1 S L48 AND STRUT
L50           15 S L47,L49
L51           34 S L35,L50
L52           27 S L51 AND ?POLYM?
L53            9 S L51 AND ?BIODEGRAD?
L54            5 S L51 AND ?BIOCOMPAT?
L55           10 S L52 AND L53,L54
L56            4 S L51-L55 AND (PY<=1992 OR PRY<=1992 OR AY<=1992)
L57           26 S L26-L35 AND (PY<=1992 OR PRY<=1992 OR AY<=1992)
L58           22 S L57 NOT L51
                 SEL DN AN 1 3 10 11
L59            4 S E1-E12
L60            8 S L56,L59 AND L3-L59
L61           30 S L51 AND L3-L50,L52-L59 NOT L60

     FILE 'HCAPLUS' ENTERED AT 09:25:17 ON 20 JAN 2004
L62            1 S US20020013275/PN
L63            1 S L62 AND L3-L59 NOT L60,L61

     FILE 'MEDLINE' ENTERED AT 09:28:20 ON 20 JAN 2004
L64         8866 S ?RESTENOS?
                 E RESTENOSIS/CT
                 E E4+ALLL
                 E E3+ALL
                 E E2+ALL
                 E E10_ALL
                 E CORONARY STENOSIS/CT
                 E E3+ALL
L65         1900 S E10+NT
                 E RESTENOSIS/CT
                 E E5+ALL
                 E E2+ALL
L66         5160 S E5+NT
                 E E13+ALL
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L67        10087 S E5 OR E10+NT
                 E POSTOPERATIVE COMPLICATION/CT
                 E E4+ALL
L68        18872 S L64-L67
L69        16380 S L9
L70         1442 S L69 AND MIGRAT?
                 E MUSCLE, SMOOTH/CT
                 E E4+ALL
L71        34552 S E10+NT
L72         1530 S L71 AND MIGRAT?
L73        20529 S L64-L67,L70,L72
L74        20529 S L68,L73
L75         4500 S L74 AND STENT?
                 E STENT/CT
                 E E4+ALL
L76        16809 S E4
                 E E3+ALL
L77       205031 S E3+NT
                 E IMPLANT/CT
                 E E39+ALL
L78         9980 S E2+NT
                 E IMPLANTATION/CT
                 E E55+ALL
                 E E2+ALL
L79        27626 S E3+NT
                 E ANGIOPLASTY/CT
                 E E3+ALL
L80        26369 S E10+NT
L81        61179 S E9+NT
L82       139670 S E8+NT
                 E E5+ALL
L83       108961 S E5+NT
L84        14327 S L74 AND L76-L83
L85        14649 S L75,L84
L86        10011 S L3,L4
L87           72 S L85 AND L86
L88            0 S L87 AND PY<=1992
L89           17 S L87 NOT AB/FA
L90           55 S L87 NOT L89

     FILE 'MEDLINE' ENTERED AT 09:39:18 ON 20 JAN 2004

     FILE 'WPIX' ENTERED AT 09:39:44 ON 20 JAN 2004
L91         5593 S ?RESTENOS?/BIX
L92         1930 S STENOSIS/BIX
L93         7210 S ?STENOSIS?/BIX
L94          117 S (VASCULAR?(L)SMOOTH(L)MUSCLE(L)CELL(L)MIGRAT?)/BIX
L95         7269 S L91-L94
L96        10141 S A61P009/IC,ICM,ICS
L97          384 S A61P009/ICA,ICI
L98         1063 S (B14-F01G OR C14-F01G)/MC
L99        16264 S L95-L98
                 E ANGIOPLAST/BIX
                 E ANGIOPLAST/BI,ABEX
                 E ANGIOPLAS/BI,ABEX
L100        2231 S L99 AND E5-E26,E36
L101        1140 S L99 AND STENT?/BIX
L102         303 S L99 AND PROSTHE?/BIX
L103        1116 S L99 AND IMPLANT?/BIX
L104        1229 S L99 AND ?CATHETER?/BIX
L105         415 S L99 AND (D09-C01 OR F04-E04 OR A12-V02 OR D09-C01B)/MC
L106         236 S L99 AND (B11-C04B OR C11-C04B)/MC
L107         934 S L99 AND A61M/IC,ICM,ICS,ICA,ICI
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L108        4113 S L100-L107
                 E A61K009-52/IC,ICM,ICS
L109        1821 S E3-E13
                 E A61K009-52/ICA,ICI
L110          12 S E3-E5
                 E A61K009:52/ICI
L111           1 S E3
L112         507 S L99 AND (R410 OR R430)/M0,M1,M2,M3,M4,M5,M6
L113         323 S L99 AND (R046 OR R220)/M0,M1,M2,M3,M4,M5,M6
L114        4120 S L108,L112,L113
L115          13 S L109-L111 AND L114
L116         124 S L114 AND R052/M0,M1,M2,M3,M4,M5,M6
L117          58 S L114 AND  (B12-M10A OR C12-M10A)/MC
L118          99 S L114 AND  (B12-M10# OR C12-M10#)/MC
L119         150 S L115-L118
L120        1988 S L4/BIX
                 E TAXOL/DCN
                 E E3+ALL
L121        1132 S E2
L122          16 S L119 AND L120,L121

     FILE 'WPIX' ENTERED AT 10:33:15 ON 20 JAN 2004

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Refine Search

Search Results -

Terms	Documents
protein synthesis and L13	144192

Database:
US Pre-Grant Publication Full-Text Database
US Patents Full-Text Database
US OCR Full-Text Database
EPO Abstracts Database
JPO Abstracts Database
Derwent World Patents Index
IBM Technical Disclosure Bulletins

Search: L19

Refine Search

Recall Text | Clear | Interrupt

Search History

DATE: Tuesday, January 20, 2004 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
	DB=USPT; PLUR=YES; OP=OR		
L19	protein synthesis and l13	144192	L19
L18	substantial cytotoxicity and l13	591238	L18
L17	cytotoxicity and l13	1	L17
L16	l13 ans L15	558839	L16
L15	non-biodegrable sustained release dosage and l13	548104	L15
L14	l8 and l13	1	L14
L13	6268390.pn.	1	L13
L12	l10 and L11	0	L12
L11	non-biodegradable and l9	24	L11
L10	restenosis adj2 reduce	27	L10
L9	non-binding partner and L8	2451	L9
L8	biocompatible	18967	L8
L7	6515009.pn.	1	L7
L6	5981568.pn.	1	L6

L5	5733925.pn.	1	L5
L4	5693343.pn.	1	L4
L3	6358989.pn.	1	L3
L2	6663881.pn.	1	L2
L1	5702754.pn.	1	L1

END OF SEARCH HISTORY

Refine Search

Search Results -

Terms	Documents
L10 and L11	0

Database:
US Pre-Grant Publication Full-Text Database
US Patents Full-Text Database
US OCR Full-Text Database
EPO Abstracts Database
JPO Abstracts Database
Derwent World Patents Index
IBM Technical Disclosure Bulletins

Search: L12

Refine Search

Recall Text | Clear | Interrupt

Search History

DATE: Tuesday, January 20, 2004 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT; PLUR=YES; OP=OR			
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L11	non-biodegradable and l9	24	L11
L10	restenosis adj2 reduce	27	L10
L9	non-binding partner and L8	2451	L9
L8	biocompatible	18967	L8
L7	6515009.pn.	1	L7
L6	5981568.pn.	1	L6
L5	5733925.pn.	1	L5
L4	5693343.pn.	1	L4
L3	6358989.pn.	1	L3
L2	6663881.pn.	1	L2
L1	5702754.pn.	1	L1

END OF SEARCH HISTORY

Hit List

Clear | Generate Collection | Print | Fwd Refs | Bkwd Refs | Generate OACS

Search Results - Record(s) 1 through 10 of 24 returned.

☐ 1. Document ID: US 6677307 B2

L11: Entry 1 of 24 File: USPT Jan 13, 2004

US-PAT-NO: 6677307
DOCUMENT-IDENTIFIER: US 6677307 B2

TITLE: TGF-.alpha. polypeptides, functional fragments and methods of use therefor

DATE-ISSUED: January 13, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Twardzik; Daniel R.	Bainbridge Island	WA		
Pernet; Andre	Lake Forest	IL		
Felker; Thomas S.	Vashon	WA		
Paskell; Stefan	Bainbridge Island	WA		
Reno; John M.	Brier	WA		

US-CL-CURRENT: 514/12; 530/300, 530/402

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw De

☐ 2. Document ID: US 6663881 B2

L11: Entry 2 of 24 File: USPT Dec 16, 2003

US-PAT-NO: 6663881
DOCUMENT-IDENTIFIER: US 6663881 B2

TITLE: Therapeutic inhibitor of vascular smooth muscle cells

DATE-ISSUED: December 16, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kunz; Lawrence L.	Redmond	WA		
Reno; John M.	Brier	WA		

US-CL-CURRENT: 424/423; 424/422, 424/424, 424/425, 514/411, 514/429, 514/449, 514/773

Full | Title | Citation | Front | Review | Classification | Date | Reference | ... | Claims | KWIC | Draw De

☐ 3. Document ID: US 6599928 B2

L11: Entry 3 of 24 File: USPT Jul 29, 2003

US-PAT-NO: 6599928
DOCUMENT-IDENTIFIER: US 6599928 B2

TITLE: Therapeutic inhibitor of vascular smooth muscle cells

DATE-ISSUED: July 29, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kunz; Lawrence L.	Redmond	WA		
Klein; Richard A.	Lynnwood	WA		

US-CL-CURRENT: 514/411; 424/422, 424/484, 424/490, 514/319, 514/441, 514/449, 604/43, 604/500, 604/540, 606/194, 606/195

Full | Title | Citation | Front | Review | Classification | Date | Reference | ... | Claims | KWIC | Draw De

☐ 4. Document ID: US 6589968 B2

L11: Entry 4 of 24 File: USPT Jul 8, 2003

US-PAT-NO: 6589968
DOCUMENT-IDENTIFIER: US 6589968 B2

TITLE: Epothilone compounds and methods for making and using the same

DATE-ISSUED: July 8, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Arslanian; Robert L.	Pacifica	CA		
Carney; John R.	San Bruno	CA		
Metcalf; Brian	Moraga	CA		

US-CL-CURRENT: 514/365; 548/204

Full | Title | Citation | Front | Review | Classification | Date | Reference | ... | Claims | KWIC | Draw De

☐ 5. Document ID: US 6569441 B2

L11: Entry 5 of 24 File: USPT May 27, 2003

US-PAT-NO: 6569441
DOCUMENT-IDENTIFIER: US 6569441 B2

TITLE: Therapeutic inhibitor of vascular smooth muscle cells

DATE-ISSUED: May 27, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kunz; Lawrence L.	Redmond	WA		
Reno; John M.	Brier	WA		

US-CL-CURRENT: 424/423; 604/104, 604/507, 604/508, 604/890.1, 604/891.1, 604/96.01, 606/108, 606/159, 606/191

Full | Title | Citation | Front | Review | Classification | Date | Reference | [illegible] | Claims | KWMC | Draw De

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☐ 6. Document ID: US 6515009 B1

L11: Entry 6 of 24 File: USPT Feb 4, 2003

US-PAT-NO: 6515009
DOCUMENT-IDENTIFIER: US 6515009 B1

TITLE: Therapeutic inhibitor of vascular smooth muscle cells

DATE-ISSUED: February 4, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kunz; Lawrence L.	Redmond	WA		
Klein; Richard A.	Lynnwood	WA		

US-CL-CURRENT: 514/411; 514/319, 514/324, 514/422, 514/428, 514/499

Full | Title | Citation | Front | Review | Classification | Date | Reference | [illegible] | Claims | KWMC | Draw De

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☐ 7. Document ID: US 6491938 B2

L11: Entry 7 of 24 File: USPT Dec 10, 2002

US-PAT-NO: 6491938
DOCUMENT-IDENTIFIER: US 6491938 B2

TITLE: Therapeutic inhibitor of vascular smooth muscle cells

DATE-ISSUED: December 10, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY

Kunz; Lawrence L.	Redmond	WA
Reno; John M.	Brier	WA

US-CL-CURRENT: 424/423; 435/975, 604/890.1, 604/891.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Draw De

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☐ 8. Document ID: US 6458889 B1

L11: Entry 8 of 24 File: USPT Oct 1, 2002

US-PAT-NO: 6458889
DOCUMENT-IDENTIFIER: US 6458889 B1
**** See image for Certificate of Correction ****

TITLE: Compositions and systems for forming crosslinked biomaterials and associated methods of preparation and use

DATE-ISSUED: October 1, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Trollsas; Olof Mikael	Los Gatos	CA		
Wallace; Donald G.	Menlo Park	CA		
DeLustro; Frank A.	Belmont	CA		

US-CL-CURRENT: 525/54.1; 525/419, 525/420, 525/425

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWMC | Draw De

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☐ 9. Document ID: US 6448054 B1

L11: Entry 9 of 24 File: USPT Sep 10, 2002

US-PAT-NO: 6448054
DOCUMENT-IDENTIFIER: US 6448054 B1

TITLE: Purposeful movement of human migratory cells away from an agent source

DATE-ISSUED: September 10, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Poznansky; Mark C.	Charlestown	MA		
Luster; Andrew T.	Wellesley	MA		
Scadden; David T.	Weston	MA		

US-CL-CURRENT: 424/184.1; 424/85.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | ... | Claims | KWIC | Draw De

☐ 10. Document ID: US 6416738 B1

L11: Entry 10 of 24 File: USPT Jul 9, 2002

US-PAT-NO: 6416738
DOCUMENT-IDENTIFIER: US 6416738 B1
** See image for Certificate of Correction **

TITLE: Pretargeting methods and compounds

DATE-ISSUED: July 9, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Theodore; Louis J.	Lynnwood	WA		
Axworthy; Donald B.	Brier	WA		
Reno; John M.	Brier	WA		

US-CL-CURRENT: 424/9.2; 424/1.49, 424/178.1, 424/179.1, 424/184.1, 424/194.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | ... | Claims | KWIC | Draw De

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☐ 11. Document ID: US 6358989 B1

L11: Entry 11 of 24 File: USPT Mar 19, 2002

US-PAT-NO: 6358989
DOCUMENT-IDENTIFIER: US 6358989 B1

TITLE: Therapeutic inhibitor of vascular smooth muscle cells

DATE-ISSUED: March 19, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kunz; Lawrence L.	Redmond	WA		
Klein; Richard A.	Edmonds	WA		
Reno; John M.	Brier	WA		

US-CL-CURRENT: 514/411; 424/402, 424/423, 424/443, 424/445, 424/446, 424/447, 604/890.1, 604/891.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | ... | Claims | KWMC | Draw De

☐ 12. Document ID: US 6306421 B1

L11: Entry 12 of 24 File: USPT Oct 23, 2001

US-PAT-NO: 6306421
DOCUMENT-IDENTIFIER: US 6306421 B1
** See image for Certificate of Correction **

TITLE: Therapeutic inhibitor of vascular smooth muscle cells

DATE-ISSUED: October 23, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kunz; Lawrence L.	Redmond	WA		
Reno; John M.	Brier	WA		

US-CL-CURRENT: 424/423; 424/424, 424/425, 514/411, 514/429, 514/449, 514/773

Full | Title | Citation | Front | Review | Classification | Date | Reference | ... | Claims | KWIC | Draw De

☐ 13. Document ID: US 6268390 B1

L11: Entry 13 of 24 File: USPT Jul 31, 2001

US-PAT-NO: 6268390
DOCUMENT-IDENTIFIER: US 6268390 B1
**** See image for Certificate of Correction ****

TITLE: Therapeutic inhibitor of vascular smooth muscle cells

DATE-ISSUED: July 31, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kunz; Lawrence L.	Redmond	WA		

US-CL-CURRENT: 514/411; 514/319, 514/441, 514/449, 604/508

Full | Title | Citation | Front | Review | Classification | Date | Reference | ... | Claims | KWIC | Draw De

☐ 14. Document ID: US 6171857 B1

L11: Entry 14 of 24 File: USPT Jan 9, 2001

US-PAT-NO: 6171857
DOCUMENT-IDENTIFIER: US 6171857 B1
**** See image for Certificate of Correction ****

TITLE: Leucine zipper protein, KARP-1 and methods of regulating DNA dependent protein kinase activity

DATE-ISSUED: January 9, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hendrickson; Eric A.	Providence	RI		

US-CL-CURRENT: 435/325; 435/252.1, 435/320.1, 536/23.1, 536/23.5, 536/24.3, 536/24.31, 536/24.33

Full | Title | Citation | Front | Review | Classification | Date | Reference | ... | Claims | KWIC | Draw De

☐ 15. Document ID: US 6171609 B1

L11: Entry 15 of 24 File: USPT Jan 9, 2001

US-PAT-NO: 6171609
DOCUMENT-IDENTIFIER: US 6171609 B1

**** See image for Certificate of Correction ****

TITLE: Therapeutic inhibitor of vascular smooth muscle cells

DATE-ISSUED: January 9, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kunz; Lawrence L.	Redmond	WA		

US-CL-CURRENT: 424/422; 424/484, 424/490, 606/194, 606/195, 623/1.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | ... | Claims | KWIC | Draw De

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☐ 16. Document ID: US 6075010 A

L11: Entry 16 of 24 File: USPT Jun 13, 2000

US-PAT-NO: 6075010
DOCUMENT-IDENTIFIER: US 6075010 A
**** See image for Certificate of Correction ****

TITLE: Small molecular weight ligand-hexose containing clearing agents

DATE-ISSUED: June 13, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Theodore; Louis J.	Lynnwood	WA		
Axworthy; Donald B.	Brier	WA		
Reno; John M.	Brier	WA		

US-CL-CURRENT: 514/23; 514/24, 514/25, 514/54, 514/61, 514/62

Full | Title | Citation | Front | Review | Classification | Date | Reference | ... | Claims | KWIC | Draw De

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☐ 17. Document ID: US 6074659 A

L11: Entry 17 of 24 File: USPT Jun 13, 2000

US-PAT-NO: 6074659
DOCUMENT-IDENTIFIER: US 6074659 A
**** See image for Certificate of Correction ****

TITLE: Therapeutic inhibitor of vascular smooth muscle cells

DATE-ISSUED: June 13, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY

Kunz; Lawrence L.	Redmond	WA	
Klein; Richard A.	Lynnwood	WA	
Reno; John M.	Brier	WA	
Grainger; David J.	Cambridge		GB
Metcalfe; James C.	Cambridge		GB
Weissberg; Peter L.	Cambridge		GB
Anderson; Peter G.	Birmingham	AL	

US-CL-CURRENT: 424/423; 424/424, 424/425, 514/411, 514/429, 514/773

Full | Title | Citation | Front | Review | Classification | Date | Reference | ... | Claims | KWIC | Draw De

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☐ 18. Document ID: US 5981568 A

L11: Entry 18 of 24 File: USPT Nov 9, 1999

US-PAT-NO: 5981568
DOCUMENT-IDENTIFIER: US 5981568 A
**** See image for Certificate of Correction ****

TITLE: Therapeutic inhibitor of vascular smooth muscle cells

DATE-ISSUED: November 9, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kunz; Lawrence L.	Redmond	WA		
Klein; Richard A.	Edmonds	WA		
Reno; John M.	Brier	WA		

US-CL-CURRENT: 514/411; 514/319, 514/324, 514/422, 514/428, 514/499

Full | Title | Citation | Front | Review | Classification | Date | Reference | ... | Claims | KWIC | Draw De

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☐ 19. Document ID: US 5858990 A

L11: Entry 19 of 24 File: USPT Jan 12, 1999

US-PAT-NO: 5858990
DOCUMENT-IDENTIFIER: US 5858990 A

TITLE: Fas ligand compositions for treatment of proliferative disorders

DATE-ISSUED: January 12, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Walsh; Kenneth	Carlisle	MA		

US-CL-CURRENT: 514/44; 435/320.1, 435/375, 435/377, 435/6, 435/69.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw De

☐ 20. Document ID: US 5811447 A

L11: Entry 20 of 24 File: USPT Sep 22, 1998

US-PAT-NO: 5811447
DOCUMENT-IDENTIFIER: US 5811447 A
**** See image for Certificate of Correction ****

TITLE: Therapeutic inhibitor of vascular smooth muscle cells

DATE-ISSUED: September 22, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kunz; Lawrence L.	Redmond	WA		
Klein; Richard A.	Lynnwood	WA		
Reno; John M.	Brier	WA		
Grainger; David J.	Cambridge			GB2
Metcalfe; James C.	Cambridge			GB2
Weissberg; Peter L.	Cambridge			GB2
Anderson; Peter G.	Birmingham	AL		

US-CL-CURRENT: 514/411

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